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PLACENTAL FUNCTION AND FOETAL DEATH

(1) Urinary Gonadotrophin Titration Test in Early Pregnancy

(2) Urinary Oestriol Excretion Test in Advanced Pregnancy

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THE production of gonadotrophic and oestrogenic hormones in the placenta does not run parallel. After the implantation of the ovum an inundation of the body with gonadotrophin occurs (Aschheim and Zondek, 1928). The peak of production and elimination takes place between the 40th and 80th day after nidation (Browne and Venning, 1936; Evans, Kohls and Wonder, 1937), then the amount drops rather considerably and is maintained at a low and steady level from the 4th month on until termination of pregnancy (Aschheim and Zondek, 1928). The urinary excretion of oestrogenic hormone shows quite a different curve. It increases very slowly during the first 4 months of pregnancy and from then on rises continuously until term (Aschheim and Zondek, 1928).

The mass elimination of gonadotrophic and oestrogenic hormones in the urine makes it possible to investigate the function of the placenta and to draw conclusions on the life or death of the foetus. In the majority of the cases death of the foetus is secondary, the placenta dying first, with consequent death of the child. In some exceptional cases the death of the foetus is primary with a surviving placenta (Zondek, 1947).

PLACENTAL FUNCTION AND FOETAL DEATH IN EARLY PREGNANCY

In the first 4 months of pregnancy the urinary gonadotrophin-titration test has been found reliable to determine placental function (Zondek, Sulman and Black, 1945, 1948). The morning urine is tested on three infantile 30 g. rats in regard to its contents of 500, 1,000 and 5,000 H.U. per litre respectively (H.U.=hyperaemia unit*). Rat 1 is injected with 2 ml. urine (twice

* There are a number of methods for the determination of gonadotrophic hormone: weight increase of the uterus in infantile mice and rats; hyperaemia reaction of the ovaries of infantile rats; oestrus reaction of infantile mice and rats; follicle haematomata (blood points) in infantile mice; formation of corpora lutea in infantile mice and rats; also follicle haematomata in mature rabbits after intravenous injection of the hormone.

The fastest reaction takes place in the male frog by proof of spermatozoa in urine (in the course of a half to one hour). The sensitivity to gonadotrophic hormone seems to vary in different frog strains. South American frogs (*Bufo arenarum* Hensel), which served Galli-Mainini for the discovery of his test, seem to react steadily (B. Houssay) and may be well suited for the titration test. Lately, Hon and Morris (1955) have recommended the common North American male toad, *Bufo americanus*, for the titration of chorionic gonadotrophin. They found that all pregnancies with titres of less than 3,000 international units per 24 hours from 50 to 90 days after the first day of the last normal menstrual

TABLE I

Rat 1 2×1 ml. of Urine=500 H.U./L.	Rat 2 2×0·5 ml. of Urine=1,000 H.U./L.	Rat 3 2×0·1 ml. of Urine=5,000 H.U./L.	Placental Function	Foetus
+	+	+	Normal	Alive
+	+	−	Disturbed? Repeat reaction	In danger
+	−	−	Disturbed. Repeat reaction	Little hope
−	−	−	Ceased	Dead

1 ml.) in the interval of one hour; rat 2 with 2×0·5 ml. and rat 3 2×0·1 ml. The rats are killed with ether 16–21 hours after the last injection of the urine and the ovaries inspected.

If the urine shows a content of 5,000 H.U. (rat 3) we may assume normal placental function with a live foetus. If only 1,000 H.U. (rat 2) are present the function is apparently disturbed. If 500 H.U. (rat 1) only are detectable there is little hope for the life of the foetus. If less than 500 H.U. are traceable in the urine it proves the death of the foetus. It must be stressed that reliance should never be placed on *one* reaction only, but the test should be repeated at least twice, or better three times, before a decision is reached for surgical interference with pregnancy. The placental function may be temporarily disturbed, i.e., there may be a reversible dysfunction of the placenta. Only in the case of irreversible dysfunction of the placenta should all hope for the preservation of pregnancy be abandoned (Table I).

The reversible dysfunction is recognizable by the rise of the hormone titre in repeated tests, whereas the drop of the hormone titre indicates an irreversible functional disturbance.

During the peak period (40th–48th day after implantation), the use of the gonadotrophin test for the diagnosis of disturbed pregnancy requires some caution, since a value indicating a live foetus, if obtained outside the peak period, may indicate the death of the foetus if taken during the peak period. The finding of less than 5,000 or 1,000 H.U./L. during the peak period shows an enormous decrease in hormone production and hence points to foetal death with even greater certainty than if the same value were obtained outside this period. Therefore it is possible to assume a foetus to be alive in the peak period, while the foetus is in fact dead. No clinical importance must be attached to this matter, because no live pregnancy will be interrupted.

PROGNOSIS IN THREATENED ABORTION WITH THE AID OF THE GONADOTROPHIN TITRATION TEST

Our former results (Zondek, Sulman and Black, 1945, 1948) are supplemented by the findings in cases of threatened abortion. We consider it important to have a method at our disposal which will strengthen our decision whether to be active or expectant in the treatment of threatened abortion with bleeding. By too early active treatment we may endanger a still viable pregnancy, while a too extended treatment in patients with a dead placenta will result in long bed rest and expensive treatment to no avail.

period ended in abortion. Whereas in the hyperaemia test in rats the native urine can be injected, the gonadotrophin for the frog test must be extracted from the urine by absorption on Kaolin and elution with 0·1 N-Sodium hydroxide. We consider this a disadvantage against the very simple test in rats; therefore we use the hyperaemia-reaction on the ovaries of infantile rats as has been recommended by Reiprich, Walker and Walker, Kelso, Frank and Berman, and others.

Several strains of rats may differ from one another in their ovarian response to gonadotrophin and this requires consideration. Our strain is reliable for testing placental function by titration of 500–5,000 H.U./L., but other rats with more or less sensitivity towards gonadotrophin may require smaller or higher quantities of urine for injection. We induce the hyperaemia-reaction after 24 hours on the ovaries of our strain—(on at least 5 of 10 injected infantile 30 g. rats)—with 1 international unit of chorionic gonadotrophin, by which the sensitivity of other strains of rats compared to ours can be determined. We use as standard "APL" (Ayerst, McKenna and Harrison), where 1 ampoule contains 20,000 I.U. of chorionic gonadotrophin.

During 5 years (1950–1954 inclusive), 1,025 cases of abortion have been treated in our department. The vast majority were clear-cut cases with an open cervix, with placental tissue in the cervix or incomplete abortion where the necessity for active treatment was obvious. In only 78 cases out of 1,025 (7·6 per cent) were we in need of the titration test. These 78 patients constitute the "borderline" cases, leaving the physician with the difficult decision whether he should empty the uterus, because the main and sometimes the only symptom is bleeding.*

Based on positive tests we have treated 10 patients conservatively with rather severe or long continued bleeding where we otherwise would probably have interrupted pregnancy. One pregnancy in the 2nd month with 8-day-long bleeding, 3 pregnancies in the 3rd month with bleedings lasting from 2 to 14 days, 5 pregnancies in the 4th month with bleeding from 2 to 20 days, and one pregnancy in the 5th month with 5-day-long bleeding, were saved. In spite of bleeding lasting up to 20 days, the positive test alone encouraged us to treat these cases conservatively (Table II). The

TABLE II

Month of Pregnancy	Number of Cases	Days of Bleeding
2	1	8
3	3	2, 2, 14
4	5	2, 2, 9, 12, 20
5	1	5

gonadotrophin-titration test enables us to judge the function of the placenta and by this we can preserve some pregnancies which, by clinical observation alone, would be sacrificed. In very rare cases of primary death of the child (Zondek, 1947), the foetus may be dead in spite of a positive test. In such instances there is no danger of sacrificing a live foetus, but merely of not interrupting a pregnancy with a dead foetus.

PLACENTAL FUNCTION AND FOETAL DEATH IN ADVANCED PREGNANCY

In the 4th to 5th month of pregnancy the gonadotrophin test becomes less reliable, because of the considerable decrease of production and excretion of chorionic gonadotrophin during this period. Fortunately, the placental production of oestrogenic hormone increases at this time and this gives us the possibility to use the determination of this hormone as a functional test. The oestrogen test is in principle to be preferred to the gonadotrophin test, because the titre of oestrogens in blood and urine drops much faster than that of gonadotrophin in dysfunction of the placenta. The gonadotrophic hormone is a protein hormone with a high molecular weight (about 100,000), and from this apparently arises the fact that the elimination in the urine takes several days (4–5). The oestrogenic hormone is a steroid hormone with a molecular weight of about 300, with a much faster excretion (12–36 hours). In 1933, Spielmann, Goldberger and Frank observed a steep drop of the oestrogen titre in the maternal blood in cases of placental death. They regarded 1 M.U. of oestrogens in 40 ml. blood as an indication of normal placental function. The hormone must be extracted from the blood and is tested in one mouse only, therefore implying a considerable source of error. One analysis is hardly enough to decide the important problem of foetal death, therefore 40 ml. of blood must be taken from the patient several times. This method, as far as we gather from the literature, has not been accepted.

A drop in the urinary oestrogen titre (total oestrogen), determined by bioassay, which one of us (Z.) has tried over the course of many years, did not lead to conclusive results in the diagnosis of placental dysfunction.

OESTRIOL EXCRETION TEST

During pregnancy oestriol is produced in the placenta† in large quantities and about 90 per cent of the oestrogens—on a basis of weight—are excreted in the urine in the form of oestriol

* Details will be reported elsewhere.

† By chromatographic isolation Mitchell (1952) found 3 γ-oestrone, 1 γ-oestradiol and 10 γ-oestriol in 100 g. of hydrolyzed placental tissue. These figures agree with those obtained by Huffman, Thayer and Doisy (1940) who worked with more than 400 kg. of placenta. Diczfalusy (1953) estimated in 100 g. of full-term human placenta 5 γ of oestrone, 0·46 γ of oestradiol and 17 γ of oestriol.

(Doisy and Thayer, 1931; Collip, Browne and Thompson, 1932; Marrian, 1935). This oestrogen possesses, however, a relatively very weak biological activity (ca. 1/100 of oestrone and 1/500 of oestradiol) thus rendering its estimation by bioassay difficult. On the other hand, oestrone and oestradiol, the more active oestrogens, are excreted in minute quantities (about 10 per cent), but they influence to a very high degree the biological activity of the urinary sample. If, for example, 1 litre of pregnancy urine contains 1 mg. of oestrogens (containing 0·9 mg. of oestriol), the bioassay of 0·9 mg. of oestriol will yield merely 90 M.U., while 0·1 mg. of oestrone and oestradiol will yield about 1,000 M.U. and 5,000 M.U. respectively; in other words, the very small quantities of oestrone and oestradiol exceed by far the activity of large quantities of oestriol. Thus titration of the total oestrogen by bioassay of pregnancy urine which contains a mixture of oestrogens of different activities must naturally lead to a considerable error. Even when one tries to separate the oestrogens by methods based on the Bachmann-Pettit (1941) and Mather (1942) partition scheme, the error obtained by bioassay would be considerable owing to the fact that up to 10 per cent of oestradiol may pass into the oestriol fraction and thus raise many-fold its oestrogenic titre. To meet this difficulty an improved partition method was elaborated in our laboratory in which the separation of oestriol from oestrone and oestradiol is quantitative (Finkelstein, 1952).* The method was confirmed by Brown (1955).

Even this improvement did not render the bio-estimation of oestrogens in urine practicable as a test for diagnosis of placental dysfunction for the following reasons:

(*a*) The Allen-Doisy test requires 4 days before results are obtained;

(*b*) The experimental error is in the region of ±50 per cent, thus a great variation may be encountered in the estimation of the oestrogens, e.g., titration of urine which contains 10,000 M.U. of any of the oestrogens/24 hours may give results between 5,000 and 15,000 M.U. This variation makes it difficult to distinguish between a real drop in the oestrogen concentration caused by placental dysfunction or by experimental error. This error may be eliminated by performing many parallel titrations, which is technically highly impracticable;

(*c*) Oestriol which is the main maternal oestrogen excreted during pregnancy and whose concentration rises much more steeply with the progress of pregnancy than that of the other oestrogens (cf. Fig. 1 and Table III), would be naturally the oestrogen of choice to serve as a test for disturbed pregnancy. Unfortunately, as stated above, oestriol has only a weak oestrogenic activity and therefore a bioassay would not supply much information. However, with an accurate and practicable method for oestriol estimation the titre of oestriol excretion during pregnancy might serve as a very suitable indication for placental function.

A fluorometric method for determination of oestradiol-oestrone and oestriol in pure solutions was elaborated in our laboratory by Finkelstein, Hestrin and Koch (1947) and similar methods were described by Bates and Cohen (1947) and Jailer (1947). This method was applied by Finkelstein (1952) to urinary extracts, prepared according to the previously mentioned partition technique and in this way oestriol could be determined in a matter of hours with an experimental error of ±15 per cent and a yield of 85 per cent. The fluorometric estimation of oestrogens in the urine was confirmed by Braunsberg, Osborn and Stern (1954).

PROCEDURE FOR THE SEPARATION OF OESTRIOL IN URINE AND ITS DETERMINATION BY THE PHOTOFLUOROMETRIC METHOD (FINKELSTEIN, 1952).

(a) *Separation of Oestriol in Urine*

Twenty-four hours' urine is collected.

Ten ml. are heated on an electric plate under reflux to boiling point. To the boiling urine 1·5 ml. concentrated HCl is added and the urine is hydrolyzed for 20 minutes.

* Oestriol is separated from oestrone-oestradiol by partition between benzene: petroleum ether and water. Model experiments with pure crystalline solutions of oestradiol, oestrone and oestriol have shown that in the above system the separation is complete and oestradiol or oestrone do not enter into the oestriol fraction or *vice versa*. The oestrogens added to urine were separated as completely as in pure solutions and could be recovered with a yield of ca. 85 per cent with a mean error of ±15 per cent.

After being cooled in cold water, 5·7 ml. urine are taken out and made up to 10 ml. by adding 4·3 ml. distilled water. The dilute urine is saturated with NaCl (2·7 g.) and is transferred to a separatory funnel and vigorously shaken three times with an equal amount of peroxide-free ether, freshly re-distilled.

The pooled ether extracts are washed once with 2 ml. saturated sodium bicarbonate and once with 2 ml. distilled water. The ether is then extracted three times with N/1 NaOH half of its volume each time. The pooled alkaline extracts are cooled in an ice bath and adjusted with HCl to pH 8·5. This solution is in turn extracted there times with ether, each time with half of its volume. The pooled ether extracts are washed once with 2 ml. distilled water and evaporated in an all-glass distillery apparatus to dryness. The last traces of moisture are removed under reduced pressure. The residue in the flask is dissolved in 0·3 ml. of re-distilled 96 per cent or absolute ethanol and 20 ml. of re-distilled, thiophene-free benzene after which 20 ml. of pure petroleum ether (b.p. 35°–60°) are added. This mixture is transferred to a separatory funnel and is twice extracted with distilled water, once with its equal volume and once with half of its volume. At this stage the oestrone-oestradiol and oestriol fractions are separated.

The clear benzene-petroleum ether solution which contains the oestrone+oestradiol is discarded. To the clear water phase (oestriol fraction) 5 ml. of M/15 Na_2HPO_4 are added and it is extracted three times with ether, each time with half of its volume. The pooled ether extracts are washed with 2 ml. of distilled water and evaporated to dryness under reduced pressure. The residue is dissolved in 10 ml. 50 per cent methanol which is then transferred to a separatory funnel. The methanol solution is washed once with 10 ml. re-distilled CCl_4. The methanol layer is centrifuged in order to obtain an absolutely clear solution. Five ml. of this solution are taken out with a pipette and evaporated *in vacuo* in an all-glass still. The dry residue is dissolved in 5 ml. ethanol. The clear and colourless aliquote of this solution are used for the fluorescence development.

(b) *Fluorometric Procedure*

Four tubes with ground joints (the male joint being part of the tube and the female joint part of the stopper) are filled with 0·1 ml. of the alcoholic extract under test. To two of them an accurately measured quantity of oestriol is added. The quantity of oestrogens added is so chosen as to be of similar concentration to that expected to be in the extract; for example, for late pregnancy the oestriol titre is expected to be of the order of 5,000 γ–10,000 γ/L.; an amount of oestriol calculated for these figures is added.

The tubes are then filled to the same volume with ethanol and a fifth tube filled with the same volume of ethanol serves as a blank. After evaporation of the alcohol in an electric oven at 110°–120° C., and cooling to room temperature, 1·25 ml. of 85 per cent phosphoric acid is added to each tube from a microburette. (No lubricant is used but the stopper of the burette is moistened with phosphoric acid.) The stoppers are then closed and the tubes are heated in the dark in a boiling water bath for 15 minutes. After 5 minutes the tubes are vigorously shaken, each one separately. At the end of the 15 minutes the tubes are cooled in tap water to room temperature. The contents of the tubes are then transferred to small pyrex tubes provided with the Farrand fluorometer. The fluorescence is read using a Farrand interference filter with the maximum transmission at 440 mμ in the primary position, and a Farrand interference filter with maximum transmission at 530 mμ as the photomultiplier. After taking the readings with the filter combination 440 mμ/530 mμ, the 404 mμ filter is substituted by the corning glass filter No. 5860 (maximum transmission at 365 mμ). The readings are again taken after the fluorometer is adjusted to give identical readings with both filter combinations for the blank tube. The second values subtracted from the first are used for the calculations.

The sensitivity of the instrument was in each case so adjusted as to get an almost full-scale galvanometer deflection for the tubes with the strongest fluorescence.

Calculation

The amount of the oestriol in the extract was calculated in the following way:

If the reading on the galvanometer for the tubes which contained only alcoholic extract was A, and the reading for the tubes with the extract plus the added oestriol was B, then B–A was equivalent to the known amount of the added oestriol. From this result (B–A) the amount of oestriol equivalent to the reading A was calculated. This value is easily converted into either gamma/litre or gamma/24 hours.

With the above reported methods we have once more investigated the problem of oestriol elimination during pregnancy. The determination of oestriol seemed to us very suitable as an indication for placental function (*a*) because the placenta produces mainly oestriol and (*b*) because oestriol, apparently due to its low molecular weight (288), is rapidly eliminated from the body.

First we examined the urinary oestriol titre of non-pregnant women (Zondek and Finkelstein, 1956). The titre fluctuates during the menstrual cycle with one peak before ovulation and with another peak during the pre-menstrual phase. It must be mentioned that during a normal cycle the excretion never exceeds 100 γ during 24 hours. During the first eight weeks of pregnancy the increase is insignificant, but during the 3rd month ca. 650 γ are eliminated. During the 4th month the increase has already mounted 10 times, th.m. ca. 1,000 γ/24 hours. The decisive increase takes place during the 5th month of pregnancy with an elimination of over

3,000 γ of oestriol, showing a 30-fold increase as compared with the excretion in non-pregnant women. After this a steady increase follows until the last month when ca. 10,000 γ are excreted in 24 hours (Table III and Fig. 1). These values may fluctuate in different cases of normal pregnancy in ranges of about 25 per cent.

The determination of the oestriol-titre in pregnancy-urine and especially the sudden drop of the titre has proved to be very reliable in pointing to a disturbance of placental function and consequently to foetal death (Zondek, Berlin, Goldberg and Beyth, 1953). We started our tests by examining early morning urine, and had good results; however, the use of 24-hour urine* has proved to be more suitable, especially during the last months of pregnancy and particularly in cases of toxaemia, because of the possibility of considerable fluctuations in urine excretion. It should be stressed that *one* urine analysis should never be relied upon,† but the test must be repeated twice or three times or more before a final diagnosis of foetal death is made (cf. case reports). A constant drop in oestriol excretion is characteristic of placental insufficiency.

TABLE III

Values of Oestrogens (Oestriol, Oestrone-Oestradiol) in Several Cases of Normal Pregnancy as Obtained With the Fluorometric Method (Urine/24 Hours)

Month of Pregnancy	Oestriol γ/24 hours	Oestrone-oestradiol γ/24 hours
2	170	218
3	650	
4	1,000	700
4½	2,880	
5½	4,165	980
6	5,040	1,000
7	6,800	1,000
8	8,430	1,150
9	11,000	1,700

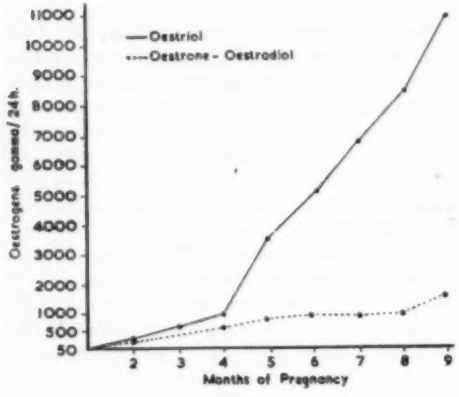

FIG. 1

Urinary excretion of oestrogens (γ/24 hours) during pregnancy.—Note the steep increase of the oestriol excretion, starting in the 5th month of pregnancy.

From the 20th week of pregnancy on, when the amount of daily elimination of oestriol is higher than 2,500 γ, the oestriol excretion test has been found reliable to determine placental function and to support the diagnosis of foetal death. We consider of importance: (*a*) the absolute oestriol titre, and (*b*) the drop in the titre. The values for the various months of pregnancy are given in Figure 1 and Table III.

Example: A urinary titre of 6,000 γ/24 hours of oestriol in the 6th or 7th month of pregnancy shows a normal placental function with living child, whereas a value of 2,000 γ at this time indicates dysfunction of the placenta. The second and third test is decisive: if the value increases from 2,000 to 4,000 γ and further, a reversible dysfunction is indicated; if, however, the value drops from 6,000 to 2,000 and under 1,000 γ/24 hours and remains under this level, the placental function is disturbed irreversibly and the child is dead.

An oestriol titre remaining below 1,000 γ= 1 mg./24 hours indicates the death of the child.

The oestriol test is of special importance in the 20th–24th week of pregnancy when the foetal heart-beat is hardly, if at all, audible. Also in the later months of pregnancy there are at times doubtful cases with hardly audible or inaudible heart sounds.

In 5 years—in a total of 11,432 pregnancies—

* We were induced to use the urine/24 hours instead of morning urine by the comment of W. J. E. Jessup during the discussion of the paper by B. Zondek (1954) at the Laurentian Hormone Conference, 1953.

† The possibility of the laboratory changing the urine in error must also be taken into consideration.

we used the oestriol test in 65 cases,* where we were unable to decide clinically whether the baby was alive or dead. We carried out concurrently the chorionic gonadotrophin excretion test to compare its value with that of the oestriol test.†

The results are summarized in Tables IV–VI.

(*a*) Table IV reports on 19 cases, where both tests yielded normal or rising values of chorionic gonadotrophin and oestriol respectively. In all cases the foetus proved to be alive. A few cases will be presented briefly:

Case 2. H. suffered from severe bleeding during the 14th week of pregnancy. The hyperaemia test on 27th May, 1954 yielded 5,000 H.U. and the oestriol test 500 γ/24 hours. On 13th June, 1954 the oestriol content rose to 1,980 γ/24 hours. In spite of continuous bleeding no active treatment was started because the placenta functioned completely. The bleeding stopped later on and pregnancy continued normally.

Case 5. N.S. had been treated in the 4th–5th month of pregnancy for continuous bleeding of varying intensity. The oestriol value was 1,450 γ/24 hours on 14th September, 1954, then fell during the next two weeks to 714 and 1,100 γ/24 hours demonstrating dysfunction of the placenta. During the next days, however, the value increased to 1,500 γ/24 hours, and after another week even to 2,700 γ/24 hours. On 5th October, 1954 we found 2,750 γ/24 hours, and on 2nd November, 1954 3,800 γ/24 hours, proving reversible placental dysfunction. Four days later pains started and a living child was born (weight, 500 g.). The child died within several hours. This and Cases 6 and 7 as well show that abortion may occur even with normal hormonal function of the placenta, showing that other causes than placental death can induce abortion.

Case 11. M. The foetal heart-beat was inaudible during the 7th month of pregnancy and foetal death was regarded as probable. The oestriol test was relatively low, 1,800 γ/24 hours. Four days later (1st July, 1953) the value was even lower (1,400 γ/24 hours); the gonadotrophin test yielded 1,000 H.U.+, 5,000 H.U.−. Based on these tests the death of the foetus could be suspected, even though the yields were still more than 1,000 γ. Four days later, however (5th July, 1953), the oestriol value rose to 5,600 γ/24 hours, demonstrating reversible placental dysfunction. At this time the heart-beat was audible. The pregnancy developed normally from then on and at term a live child was delivered.

In cases of hydramnios it is frequently difficult to hear the foetal heart. Patient Y.S. (Case 14) was admitted to our ward during the 8th month with an enormous hydramnios. The child could not be palpated. The heart-beat was not audible. Oestriol determination yielded 3,400 γ/24 hours and the gonadotrophin test=5,000 H.U. These values indicated normal placental function with a living foetus. The patient gave birth at term to a live child.

The foetal heart-beat of patient P.R. (Case 18) was inaudible, due to severe hydramnios caused by twins. The hormonal examination (5,510 γ/24 hours oestriol and 5,000 H.U. gonadotrophin) indicated normal placental function. Live twins were delivered.

In all 19 cases of Table IV the oestriol as well as the gonadotrophin test made it possible to assume normal placental function resp. reversible placental dysfunction with a living foetus. This was confirmed in all cases by clinical observation.

(*b*) Table V reports upon 19 cases in which the fate of the foetus was not clear. In these cases, the low or failing hormone titre in the urine pointed to a dead foetus, which was subsequently confirmed clinically. A few cases are described here.

In Cases 1–6 (3rd to 5th month of pregnancy) the low gonadotrophin value (500 H.U.) and the low oestriol value indicated death of the foetus. In all of them a dead foetus was expelled.

In Case 7 (H.J.) we had difficulty in diagnosing a missed abortion during the 5th month. The low gonadotrophin value (500 H.U.−) and the very low value of oestriol (73 γ/24 hours)

* After completion of this paper we had the opportunity to examine 8 more cases—from the middle of the 4th to the 9th month of pregnancy—with doubtful clinical diagnosis of foetal life or death. In one case the oestriol value on 10th October, 1955 was 2,200 γ/24 hours, whereas 3 weeks later only 94 γ/24 hours could be detected, indicating foetal death. On 5th November, a live child was born. Although we had to classify this case as an error, we nevertheless have the suspicion that the urine, sent from the department, did not belong to our patient, because the chorionic gonadotrophin also was completely negative. In the remaining 7 cases the diagnosis based on the oestriol excretion test was correct, confirming that in 3 cases the child was alive, whereas in 4 cases the child was dead.

† Investigations are at present being carried out to see whether the oestriol values are reliable enough for determining placental function in the early months of pregnancy.

TABLE IV

Cases Where the Excretion of Chorionic Gonadotrophin and of Oestriol Gave Normal or Increasing Values. The Child was Alive

No.	Name	Date	Month of Pregnancy	Gonado-trophin in H.U./L.	Oestriol γ/24 Hours	Remarks
1	G.M.	8th September, 1954	2	5,000+	170	Missed abortion? Oestriol titre
		22nd September, 1954	3	5,000+	300	increased, pregnancy continued
2	H.	27th May, 1954	3–4	5,000+	500	Severe bleeding
		13th June, 1954		5,000+	1,980	Pregnancy continued
3	V.	4th November, 1953	4	500+	800	
				1,000±		
				5,000±		
		9th November, 1953		5,000+	1,240	Pregnancy continued
4	K.R.	27th January, 1955	4–5	5,000+	2,600	
5	N.S.	14th September, 1954	4–5	5,000+	1,450	Continuous bleeding
		21st September, 1954			714	
					1,100	
		24th September, 1954			1,500	
		1st October, 1954			2,700	
		5th October, 1954			2,750	
		2nd November, 1954			3,800	
6	M.F.	15th December, 1953	5	5,000+	3,300	Bleeding, pregnancy continued
7	F.	1st December, 1952	5	5,000+	4,000	Aborted a living foetus
8	B.A.	1st January, 1953	5	5,000+	3,000	Aborted a living foetus
9	T.R.	20th December, 1954	5–6	5,000+	10,000	
10	Sh.	2nd March, 1954	6–7	5,000+	10,000	
11	M.	26th June, 1953	7–8		1,800	Foetal heart not heard
		1st July, 1953		5,000−	1,400	
				1,000+		
		5th July, 1953		5,000+	3,400	
		6th July, 1953		5,000+	4,000	
		2nd August, 1953		5,000+	5,600	Foetal heart heard
		3rd August, 1953			2,800	
		6th August, 1953			3,360	
		16th August, 1953			5,300	Pregnancy develops normally, living child born
12	E.	9th December, 1951	8	5,000+	4,300	
13	S.	5th August, 1952	8	5,000+	9,000	
14	Y.S.	27th July, 1954	8	5,000+	3,400	Hydramnios, living child born, died one month later
15	B.D.	2nd August, 1954	8	5,000+	4,400	
				5,000+	6,250	
				5,000+	6,680	
16	K.	7th December, 1952	9	5,000+	7,500	
17	T.	26th June, 1953	9	5,000+	12,000	Twins
18	P.R.	9th January, 1954	9	5,000+	5,510	Hydramnios, twins
19	B.	13th August, 1952	9	5,000+	6,000	

indicated that the placenta did not function. Subsequent clinical observation confirmed the diagnosis of missed abortion.

In cases during the last trimester (12–19), the low oestriol values showed very distinctly the death of the foetus, which fact was invariably clinically confirmed.

In Case 18 (K.) one could draw the conclusion from the very low (45 γ/24 hours) oestriol value during the 7th month of pregnancy that the placenta had stopped functioning some time ago. This was confirmed by the advanced maceration of the foetus at birth.

The reported cases show that low oestriol and

TABLE V

Cases Where the Low or Decreasing Values of Chorionic Gonadotrophin and of Oestriol Indicated Foetal Death. This was Confirmed Clinically in All Cases

No.	Name	Date	Month of Pregnancy	Gonadotrophin in H.U./L.	Oestriol γ/24 Hours	Remarks
1	E.R.	3rd May, 1955	3	500−	38	
2	B.	16th August, 1954	4	500−	88	
3	G.	12th January, 1953	4	500+	250	
				1,000−		
4	C.R.	1st April, 1955	4–5	500−	146	
5	H.	17th July, 1952	4–5	500−	335	
6	E.	27th August, 1950	5	500−	400	
7	H.J.	8th September, 1954	5	500−	73	Missed abortion
		13th September, 1954		500−	40	
8	M.N.	22nd August, 1951	6	500−	80	
9	R.	8th April, 1954	6	500−	400	
10	B.R.	28th December, 1954	6	500−	180	
11	M.M.	5th April, 1955	6	500−	130	
12	Z.	17th December, 1950	6–7	1,000+	160	
				5,000−		
		25th December, 1950		500−		
13	T.	16th August, 1950	7	500−	135	
14	S.T.	18th August, 1952	7	500−	264	
15	E.	24th November, 1952	7	500−	220	
16	A.S.	12th January, 1953	7	500+	275	
				1,000−		
17	B.T.	7th September, 1954	7	500−	1,344	
		13th September, 1954		500−	110	
18	K.	21st September, 1954	7	500−	45	Macerated foetus
19	K.	5th August, 1954	8–9	500−	90	

gonadotrophin values indicate the cessation of placental function and foetal death.

(*c*) Table VI reports on 25 cases, which prove the superiority of the oestriol excretion over the gonadotrophin excretion test to diagnose foetal life or death from the 5th month of pregnancy onwards. Some of the cases are reported here:

Patient E.R. (Case 1) has had one living child and 9 abortions. Patient was admitted in the 16th week of pregnancy, bleeding very slightly. The gonadotrophin value still yielded 5,000 H.U., but the oestriol test was low (280 γ/24 hours). One week later a macerated foetus was expelled.

Patient M.E. (Case 5) had a positive gonadotrophin test in the 5th month of pregnancy (5,000 H.U./L.+), while the oestriol test showed a low value (550 γ/24 hours). Two days later a dead foetus was expelled.

Case 9, patient Ch.T., with a history of several abortions, was in the 5th–6th month of her pregnancy. The condition of the child could not be decided upon. The gonadotrophin test carried out on 19th April, 1954 turned out to be positive (5,000 H.U.+), while the oestriol value was at that time already low (728 γ/24 hours). One week later, the gonadotrophin titre dropped (5,000 H.U.−, 1,000 H.U.+) and the oestriol value decreased to 312 γ/24 hours, demonstrating irreversible placental dysfunction. On 12th May a macerated foetus was expelled.

Cases 15 and 16 (7th and 8th month of pregnancy respectively) demonstrate normal values by the gonadotrophin test (5,000 H.U.+), whereas the oestriol test was very low (300 γ resp. 500 γ/24 hours). In both cases a macerated foetus was expelled.

Case 17 (S.H.) demonstrates on 20th and 23rd July, 1953 still 1,000 H.U./L. gonadotrophin, while the oestriol value was low (880 γ, 650 γ/24 hours). A dead child was born. This case, like many others, shows a slower urinary elimination of gonadotrophin than of oestriol.

TABLE VI

Cases Where the Oestriol Excretion Test Proved to be Superior to the Gonadotrophin Excretion Test in the Diagnosis of a Live or Dead Foetus

No.	Name	Date	Month of Pregnancy	Gonadotrophin in H.U./L.	Oestriol γ/24 Hours	Remarks
1	E.R.	20th June, 1954	4	5,000+	280	Macerated foetus
2	R.R.	26th January, 1955	4	1,000+	2,880	Pregnancy continued
				5,000−		
3	Z.	29th January, 1953	4–5	1,000+	1,260	Pregnancy continued
				5,000−		
4	S.T.	5th December, 1952	5	5,000±	350	Abortion
				1,000+		[foetus
5	M.E.	16th January, 1955	5	5,000+	550	18th January abortion of a dead
6	Z.	20th August, 1950	5–6	1,000+	3,000	Pregnancy continued
				5,000−		
7	R.	27th June, 1951	6	5,000+	250	
		12th July, 1951		5,000−	850	13th August abortion of a dead
				1,000+		foetus
		16th July, 1951		1,000+	500	
8	Sh.S.	14th November, 1952	6	1,000+	780	Dead foetus delivered
				5,000±		
9	Ch.T.	19th April, 1954	5–6	5,000+	728	
		25th April, 1954		1,000±	312	
				5,000−		
		28th April, 1954			300	
		10th May, 1954		1,000±	290	On 12th May macerated foetus
				5,000−		
10	S.L.	13th February, 1955	6	10,000+	800	Toxaemia of pregnancy
		15th February, 1955		10,000+	400	
		16th February, 1955		5,000+	625	
		21st February, 1955		5,000+	192	On 21st February macerated foetus
11	B.	27th January, 1955	6–7	500,000+	1,040	Toxaemia of pregnancy
		2nd February, 1955		50,000+	998	
		6th February, 1955		50,000+	277	6th February macerated foetus
12	M.	10th September, 1951	6–7	5,000+	1,333	Macerated foetus
13	Ch.	9th March, 1954	6–7	1,000+	680	Dead foetus
				5,000−		
14	L.N.	1951	7	5,000+	720	Dead foetus
15	R.	16th October, 1952	7	5,000+	300	Macerated foetus
16	M.R.	1951	8	5,000+	500	Macerated foetus
17	S.H.	20th July, 1953	8	1,000+	880	
				5,000±		
		23rd July, 1953		1,000+	650	Stillbirth
				5,000−		
18	S.N.	29th August, 1954	8	5,000±	350	Macerated foetus delivered
				1,000+		
19	Z.T.	25th May, 1955	8	5,000−	180	26th February macerated child
				1,000+		
20	H.A.	19th August, 1954	8	1,000+	420	Macerated foetus
				5,000−		
21	H.	6th January, 1953	9	5,000+	1,100	
		7th January, 1953		5,000+	214	
		8th January, 1953			200	8th January, 1953 macerated child
22	G.M.	25th April, 1954	9	5,000±	440	Stillbirth
				1,000+		
23	D.K.	February, 1955	9	5,000−	210	Stillbirth
				1,000+		
24	M.E.	30th August, 1950	9	1,000+	2,700	Live birth
				5,000−		
25	N.	14th September, 1954	9	5,000+	3,722	
		15th September, 1954		5,000+	1,142	16th September 3,600 g. child born with signs of maceration, placenta not degenerated

We attach importance to the oestriol test in cases of toxaemia of pregnancy. Smith and Smith reported an increased production of gonadotrophin in cases of toxaemia, while the oestrogen hormone production decreases. According to our experience only some cases of toxaemia show the above pattern of high excretion of gonadotrophin and low excretion of oestrogens; there are even cases of severe toxaemia without this discrepancy of hormonal excretion. The gonadotrophin test may lead to error in cases of toxaemia with high gonadotrophin excretion. In normal pregnancy the value of 5,000 H.U. gonadotrophin outside the peak period indicates normal placental function. In toxaemia, however, with a high urinary titre of 100,000 H.U./L. or more, the decrease to 5,000 H.U./L. will not prove normal placental function. We find in Case 10 (S.L.) during the 6th month of pregnancy on 13th February, 1955, a gonadotrophin value of 10,000 H.U./L., whereas the oestriol value amounts to 800 γ/24 hours only. The same day a macerated foetus was expelled. In spite of the cessation of placental function and death of the child, the urine was still abundant with gonadotrophin (10,000 H.U.).

Another case (11) of toxaemia during the 6th–7th month of pregnancy showed an enormous increase of gonadotrophin excretion (500,000 H.U.+); the oestriol value was 1,040 γ/24 hours. On 2nd February, 1955 the gonadotrophin content in the urine fell considerably, but still amounted to 50,000 H.U./L. The same value was found on 6th February, 1955, while the oestriol value had dropped to 277 γ/24 hours. On the same day a macerated foetus was expelled.

Only in one case (25) both hormonal tests failed when in spite of normal hormonal values a macerated foetus was born. Here the issue at hand was primary death of the child with a surviving placenta (Zondek, 1947). In contrast to the maceration of the foetus the placenta anatomically did not point to degeneration. Extraction of the placenta yielded a value of 200 M.U. of free oestrogenic hormone.

The cases, reported upon in Table VI, show that from the 5th month of pregnancy on, the oestriol test is in most cases superior to the gonadotrophin test.

Placental dysfunction. The diagnosis of placental dysfunction is based upon serial examinations of the oestriol content of the urine. Fluctuations in the urinary oestriol titre indicate reversible placental dysfunction with a living foetus, when the oestriol titre rises continuously over 1,000 γ/24 hours. If, however, the titre is low and rises only slightly above the decisive value of 1,000 γ/24 hours and then drops again, the placental dysfunction is irreversible leading to the death of the foetus. This is shown by the following 2 cases (not included in Tables IV–VI):

(1) C.C. in her 6th month of pregnancy. The urinary titre of 323 γ/24 hours (4th March, 1956) suggested a severe placental dysfunction, but a week later the titre rose to 1,200 γ and remained at this level during 7 days. A further drop, however, to 750 γ (4 days later) proved irreversible placental dysfunction. Two weeks later a macerated foetus was expelled.

(2) In another case in the 5th/6th month of pregnancy the oestriol titre fluctuated over the course of 2 weeks: 204 γ/24 hours, 1,016 γ/24 hours, 44 γ/24 hours, indicating irreversible dysfunction of the placenta. Ten days later a macerated foetus was expelled.

Discussion

We know that the placenta produces steroid hormones such as oestriol and progesterone and protein hormones such as gonadotrophin and probably also A.C.T.H. The quantitative elimination of these hormones varies during the course of pregnancy. Immediately after the implantation of the ovum a mass production of gonadotrophin occurs, while the steroid hormones (oestriol and progesterone) increase considerably only in the later months of pregnancy. The high production and elimination of gonadotrophin constitute a good method for testing the placental function during early pregnancy. The analysis of steroid hormones should be the favoured test in advanced pregnancy starting at the 20th week. To obtain a complete functional test of the placental function, one should analyze the gonadotrophin, as well as the oestriol and pregnanediol excretion. Though the various investigations on the metabolism of pregnanediol during the menstrual cycle and during pregnancy are very interesting, the values reported by

different authors seem to differ. Apparently, there has not been described as yet a reliable method for the analysis of pregnanediol. Recently, Coyle, Mitchell, Russell, and Paine (1955) have pointed in detail to the errors in the determination of urinary pregnenediol. Nevertheless several authors (Browne, Henry and Venning, 1939; Cope, 1940; Hamblen, 1941; Guterman, 1946) have reported falling titres of pregnanediol prior to abortion and as an indication of foetal death. On the other hand Delfs and Jones (1948), Kaesar and Eichenberger (1949), Mueller (1950) and others concluded that neither high, low nor falling pregnanediol excretion are of prognostic significance for predicting the fate of the ovum. In patients with toxaemia the excretion of pregnanediol gives no information on the severity of the toxaemia nor on the fate of the foetus (Trolle, 1955). Thus, pregnanediol excretion may be seen in cases of foetal death, and conversely, negligible pregnanediol excretion may be found in spite of a living foetus (Trolle, 1955).

We believe that from the 20th week on the oestriol analysis suffices as a reliable test for placental function and dysfunction leading to foetal death. The fluorometric method makes possible an exact determination of the urinary oestriol, which can be carried out in about 4–5 hours.

Summary

(1) The placental production of the sex hormones manifested by their urinary hormonal titre has been used as a test for placental function and dysfunction (reversible or irreversible).

The urinary chorionic gonadotrophin titration test is recommended as a test for the diagnosis of placental insufficiency and foetal death in early pregnancy.

The test proved to be of importance in the treatment of threatened abortion. Guided by this test 10 pregnancies were brought to term which otherwise would probably have been interrupted. The advantage of the hormonal test is twofold: to continue expectant treatment, if the test remains positive in spite of bleeding (1–3 weeks) and thus to save a pregnancy; or to shorten the period of illness and to treat actively if several tests have proved the cessation of placental function.

Since the excretion of chorionic gonadotrophin—probably due to its high molecular weight—takes several days, the test may remain still positive in spite of an irreversible placental dysfunction. This fallacy is however not misleading, because a positive test may lead to the conservative treatment of a failed pregnancy, but not to the artificial termination of a live pregnancy. Furthermore, the hormonal test can remain positive in the rare cases of primary death of the foetus.

If a woman bleeds during the first months of pregnancy and there is no placental tissue palpable in the cervix, termination of pregnancy is not indicated so long as the test remains within normal limits. Only a falling urinary gonadotrophin titre tested by repeated examinations gives the indication for the termination of the pregnancy.

(2) The urinary oestriol titre is recommended as a method for testing the placental function in advanced pregnancy. The use of this test became possible only after the discovery of the methods cited here: (*a*) to separate oestriol quantitatively from the other urinary oestrogens, and (*b*) to determine oestriol by fluorometry. Oestriol can hardly be measured by bioassay due to its very low oestrogenic activity.

The oestriol test is reliable from about the 20th week of pregnancy and onwards. (Investigations on its value during the early months of pregnancy are being carried out at present.)

The oestriol test in advanced pregnancy is superior to the gonadotrophin titration test, because, from the 4th month of pregnancy on, the curve of production and elimination of gonadotrophin falls rapidly in contrast to the curve of oestriol, which from this period on rises continuously.

The elimination of gonadotrophin lasts several days, whereas the elimination of oestriol lasts only 24–48 hours.

In the extraction of the oestrogens from pregnancy urine, which contains ca. 90 per cent of oestriol and 10 per cent of oestrone and oestradiol, oestriol is separated from oestrone-oestradiol by partition between benzene: petroleum ether and water. A quantitative determination of oestriol is carried out by the photofluorometric method.

If the oestriol excretion test is used to diagnose foetal death, one single examination should never be relied upon; several tests are required. An oestriol titre remaining below 1,000 γ/24 hours urine indicates irreversible placental dysfunction and secondary death of the foetus. Only in very rare cases of primary foetal death with a surviving placenta can the child be dead in spite of normal oestriol values (observed in 1 case of 75).

Fluctuations in the urinary elimination of oestriol indicate dysfunction of the placenta. The rising titre indicates reversible placental dysfunction, whereas the falling titre (remaining under 1,000 γ/24 hours) proves irreversible placental dysfunction with foetal death.

In cases of toxaemia of pregnancy with high excretion of gonadotrophin, the oestriol test is of special importance. In these cases, in spite of the death of the foetus, the urinary gonadotrophin titre may still be high, while the oestriol value is already low.

The hormonal tests inform us about the dysfunction of the placenta leading to death of the foetus and abortion, but they do not explain other causes of the expulsion of the foetus.

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Addendum

In cases of hydropic placenta caused by Rh incompatibility the hormonal values seem to be inconsistent. Both tests, therefore, should be used with caution in such cases. Details will be reported later.

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ACUTE ADRENO-CORTICAL INSUFFICIENCY IN OBSTETRICS AND GYNAECOLOGY

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ACUTE adreno-cortical insufficiency is a diagnosis frequently made in retrospect at autopsy. In the majority of published cases the correct diagnosis was not entertained during life. The object of this paper is to present 4 cases that have occurred in this hospital since 1952, and to discuss the pathogenesis and aetiology of this condition. It is felt that acute adreno-cortical insufficiency, as distinct from suprarenal haemorrhage without insufficiency, presents a characteristic syndrome. It is a specific clinical entity demanding specific therapy.

The reported cases have been associated with a wide variety of conditions. The groups may be divided as follows:

(1) Patients with pre-existing hypocorticism who develop acute adrenal insufficiency. The previous hypocorticism may be overt, as in known cases of Addison's disease, or unsuspected. The cause of this hypocorticism may be disease or it may be iatrogenic.

(2) A previously normal individual who develops acute insufficiency.

The patient with Addison's disease who meets with a stress and passes into crisis belongs to the first group. The clinical importance of the individual with unsuspected hypocorticism is emphasized by Forsham and Thorn (1955) and in this group are some of the patients whose first evidence of deficiency is sudden unexplained operative and post-operative shock. Taylor and Essig (1953) record 6 such cases.

Iatrogenic insufficiency may result from the surgical ablation of the adrenals for hypertension or advanced carcinoma, but more commonly from suppression of the adrenal cortex by the prolonged administration of cortisone or hydrocortisone for such conditions as rheumatoid arthritis. The danger of this occurrence has been stressed by Sayers and Sayers (1947), Rukes, Orr and Forsham (1954), Hart (1955) and Forsham and Thorn (1955). Cases of shock and death in this group have been recorded by Salassa *et al.* (1953) and Lewis *et al.* (1953). The 3 patients in these reports had been receiving cortisone for rheumatoid arthritis.

The causes of acute adreno-cortical insufficiency in previously eucorticoid individuals are legion. Initially most attention was directed to the Waterhouse-Friderichsen syndrome (Waterhouse, 1911; Taylor and Keane, 1943) but it became apparent that this syndrome was not peculiar to meningococcal septicaemia, but could occur in a wide variety of situations from haemolytic streptococcal infections to an experimentally induced generalized Shwartzman reaction (Selye, 1950). Acute cortical insufficiency has been recorded in neonatal deaths, lobar pneumonia and carcinoma of the prostate (Hall and Hemken, 1936), after cardiac surgery (Black and Harken, 1954), ulcerative colitis (Owen and Coleman, 1955), abdominal and chest injuries (Sevitt, 1955), head injuries (Levene, 1955). In pregnancy the condition has been associated with an otherwise normal gestation, with pre-eclampsia and eclampsia, infection, hyperemesis gravidarum and Caesarean section (Keele and Keele, 1942; Hurter, 1946; Dewhurst, 1951; MacGillivray, 1951; Crawford, 1951; Peterson and Goldzieher, 1953).

This list of conditions is not meant to be exhaustive, but merely to indicate the wide variety of associated and precipitating factors. As so many different initiating factors produce the same end result, it is not improbable that

they do this by a final common mechanism. This will be discussed more fully below.

Changes in the Adrenal Cortex

The patients who die in acute failure and are known cases of Addison's disease show the pathology of that disease; either tuberculosis of the gland or "primary" atrophy.

In those cases whose cortical deficiency was caused by cortisone therapy, the glands are smaller and lighter than normal. This is due to cortical atrophy involving mainly the zona fasciculata. The medulla is not involved. There is loss of lipoid substance from the cortex and the cytoplasm is eosinophilic and granular. The small size is due to shrinkage of the cells rather than diminution in number (Salassa *et al.*, 1953; Stoner and Whiteley, 1954).

In the group described by Taylor and Essig (1953), in whom the hypocorticism was not suspected, similar changes to those described above were seen, although none of the patients had received cortisone.

The changes in the glands of previously normal individuals who die of adrenal failure are quite different. There is increased size of the cortex, loss of lipoid substance, transudates in the cell columns and multiple scattered thromboses. Pseudo-tubule or lumina formation is especially common and haemorrhages spreading centrifugally from the reticularis may occur (Selye, 1950; Forsham and Thorn, 1955). The haemorrhages when present may be microscopic or so extensive that the whole gland including the medulla is involved, the capsule containing a sac of blood. The changes may be bilateral or predominantly unilateral. Adrenal vein thrombosis has been emphasized by Hall and Hemken (1936) and Keele and Keele (1942) but in the majority of cases this is not a feature. Widespread necrosis may occur without haemorrhage. However it should be emphasized that severe lipoid depletion, pseudo-tubule formation, ischaemic necrosis and haemorrhage have been found post-mortem in patients in whom there was no clinical or haematological evidence of adrenal failure before death. Symington *et al.* (1955) stress the care that must be "exercised in attempting to correlate biological activity with a static histological picture". Perhaps it is not stretching analogy too far to compare the clinical and post-mortem findings of acute adreno-cortical failure with those of diabetic coma, where a most impressive clinical picture leaves little evidence, with present autopsy methods, of the metabolic storm that kills the patient.

Report of Cases

Case 1, Mrs. U.B., age 25 years

This patient was admitted to this hospital on 18th November, 1953. She was in the thirty-fifth week of her first pregnancy. The patient was a known diabetic of 14-years duration and was currently well stabilized on soluble insulin, 40 units, protamine zinc insulin, 40 units before breakfast and soluble insulin 10 units before tea. Her blood pressure was 120/75 and there was no protein in the urine. On 19th November the non-fasting blood sugar was 159 mg. per cent and on 24th November it was 138 mg. per cent.

On 25th November at 2 p.m. an elective lower segment Caesarean section was performed. Blood loss was not excessive and no blood was given. On returning to the ward she was conscious and her pulse was 90. At 6 p.m. the nurse could not feel the patient's pulse. When seen from the end of the bed the patient looked quite well, apart from slight cyanosis of the lips, and apart from the incisional pain she felt well. However the radial pulse could not be felt and the blood pressure was unrecordable. The heart rate was 180 per minute. There was only a normal amount of vaginal loss and the fundus was firm. The first diagnosis entertained was paroxysmal tachycardia. An electrocardiograph showed sinus tachycardia with a rate of 210 per minute. Digoxin, 0·5 mg., was given intravenously at 7.45 p.m. and repeated at 8.30 p.m. The pulse and blood pressure were still unrecordable. The patient however still looked in surprisingly good condition.

At 1.30 a.m. there was still no blood pressure and the patient's condition was deteriorating. She was becoming restless and the skin was now cold and becoming blotchy. For the first time a diagnosis of adrenal failure was entertained. Hydrocortisone was not available at that time. Whole adrenal extract (Eschatin) was given intravenously in a dose of 20 ml. and an intravenous drip of noradrenalin in 5 per cent glucose in 1/5 normal saline was commenced. At the same time 100 mg. of cortisone acetate was given intramuscularly. By 2 a.m. the blood pressure could be recorded for the first time since 6 p.m. It varied between 130/90 and 110/70.

The eschatin was repeated in the same dosage of 20 ml. every 2 hours. At 6.30 a.m. the noradrenalin drip blocked and the blood pressure immediately fell to 70/30. The drip was restarted.

By 7 a.m. increasing amounts of noradrenalin were needed to maintain a blood pressure and it was very difficult to keep it above 80 mm. systolic. At about the same time the patient developed a diffuse purpuric rash over the face. The blood glucose at this time was 177 mg.

per cent and the serum electrolytes were: Chloride 107 meq. per litre, CO_2 combining power 11 meq. per litre, sodium 130 meq. per litre, potassium 4·5 meq. per litre. The blood urea was 57 mg. per cent.

At 8 a.m. the patient was catheterized and 30 ml. of urine were obtained, the first since the operation.

During the morning the quantity of noradrenalin was constantly increased. At 2 p.m. the purpuric rash had spread to involve the whole body and the blood pressure could not be kept above 70 systolic. At this time a further 100 mg. of cortisone acetate was given intramuscularly. The patient was now wildly confused, with icy cold skin and blotchy cyanosis; peripheral circulation was almost absent. The blood pressure continued to fall and at 5.30 p.m. the patient died.

Autopsy. This was performed by Dr. Mary Heseltine. Apart from the puerperal uterus the only significant abnormalities were of the adrenal glands and the pituitary. The adrenals were bright red and haemorrhagic and on section contained haemorrhages throughout the cortex and medulla. The pituitary was a rich red colour. Unfortunately the blocks were lost before sections could be cut.

Comments

There was a delay of 7 hours before the nature of this patient's shock was appreciated. Once it was appreciated too much reliance was placed on intramuscular cortisone as the slowness of utilization was not realized, and insufficient amounts of eschatin were given. It was a case of too little much too late.

The outstanding feature of this case was the general appearance of the patient when she had no recordable blood pressure. The warmth of the skin, the cyanosis of the lips and the mental clarity in the initial stages were quite remarkable. The development of purpura in this case is noted as it is unusual in this syndrome occurring in pregnancy.

Case 2, Mrs. A.C., age 33 years

This patient was a routine admission to the gynaecological wards of this hospital on the afternoon of 30th May, 1955. She was suffering from myomata uteri. The pre-operative haemoglobin was 9·4 gm. per cent. A myomectomy was performed at 9 a.m. on the 31st May. The anaesthetic used was pentothal sodium/tubocurarine/nitrous oxide/oxygen, and 1,000 ml. of whole blood were given during the operation because of the low haemoglobin. On returning to the ward at 10.30 a.m. the patient was conscious and morphine sulphate, gr. ¼, was given subcutaneously. On that day and the following her pulse did not rise above 90 per minute. At 5.30 p.m. on the 1st June, she complained of upper abdominal pain, most severe in the epigastrium. This became increasingly severe. At 6.30 p.m. her pulse in the wrist could not be felt, nor could the blood pressure be recorded. She was warm, with marked cyanosis of the lips, fingers and ears. The jugular venous pressure was not raised and there were no abnormal signs in the chest. There was generalized abdominal tenderness, maximal in the epigastrium, but no vaginal bleeding and no evidence of retroperitoneal or intraperitoneal bleeding. The patient looked quite unlike a case of haemorrhagic shock.

The first diagnosis was that of pulmonary infarction, despite the fact that only 36 hours had elapsed since operation. Thirty mg. of methedrine intravenously produced no discernible effects on the blood pressure so an intravenous drip containing 16 mg. of noradrenalin in 500 ml. of 5 per cent glucose in distilled water was set up. It was necessary to run this at 25 drops per minute to obtain a recordable blood pressure and this was stabilized at 110/80. This rate of flow was continued during the night and early the following morning. A full blood-count on the morning of 2nd June showed:

Red cells	4·7 million.	
Haemoglobin	10·8 g. per cent.	
White cells	27,200.	
	Total neutrophils	78 per cent.
	Lymphocytes	11 per cent.
	Monocytes	8 per cent.
	Eosinophils	2 per cent.
	Basophils	1 per cent.

At 11 a.m. on 2nd June the blood pressure again became unrecordable despite increasing the amount and rate of noradrenalin infusion. The patient now looked moribund, with blotchy cyanosis and very slow peripheral blood flow. In view of the developing unresponsiveness to noradrenalin and because there was no evidence of bleeding a provisional diagnosis of acute adreno-cortical failure was made. No hydrocortisone was immediately available so 40 ml. of whole cortical extract (Eschatin) was given intravenously together with 10 mg. of DOCA intramuscularly and 50 mg. of cortisone acetate intramuscularly. The noradrenalin was continued and a further 40 ml. of eschatin was added as a side drip. Within half an hour the blood pressure had risen to 110/70 but the patient still looked perilously ill. At 12.45 p.m. hydrocortisone was obtained and 100 mg. as the free alcohol was set up intravenously, diluted in 500 ml. of 5 per cent glucose in normal saline and run in over a period of 4 hours. By the end of this time the patient looked very much better and the amount of the noradrenalin was reduced to 8 mg. to each 500 ml. of solution. Cortisone acetate 100 mg. was given intramuscularly every 8 hours.

This regime was continued on the 3rd June. Hydrocortisone 100 mg. was given over an 8-hour period by slow intravenous drip and the noradrenalin was reduced to 4 mg. to each 500 ml. of solution running at 20 drops per minute. The blood pressure was stable at 110/70, the patient felt tolerably well and the urinary output was adequate.

On the 4th June it was found that the noradrenalin could be completely withdrawn without the blood pressure falling. Cortisone acetate was continued intra-

muscularly in a dosage of 50 mg. every 8 hours. The white cells were 26,000 with 1 per cent lymphocytes and no eosinophils.

On the following day, 5th June, the patient suddenly developed an attack of acute pulmonary oedema. X-ray examination of the lungs showed the typical "bats wing" mottling. This fortunately rapidly responded to treatment. The cortisone was continued in diminishing dosage for several more days and was then withdrawn completely. The patient was now quite well, out of bed, with a blood pressure of 110/70. She was discharged from hospital on the 18th June, 1955. Mrs. C. was last seen early in 1956 and remains quite well.

Comment

Again there was the initial appearance of warmth, cyanosis and apparent well being, associated with an unrecordable blood pressure. Unfortunately the eosinophil count in this patient was not direct, so that even although there was a disappearance of the eosinophils from the differential count after the initiation of specific therapy, the fields counted may have not been typical. More significant in this type of count is the fall of the lymphocytes where the number of cells dealt with was much more numerous. The initial response to large quantities of noradrenalin in this patient, followed by the development of unresponsiveness, which in turn was reversed by exogenous corticoids, is typical of this condition.

This patient was treated with too much enthusiasm. The dosage of both the cortisone and hydrocortisone was more than necessary, and this combined with a high sodium intake during the intravenous therapy undoubtedly caused the pulmonary oedema.

The pain in this patient was the presenting and initially the only symptom. It was similar in character to that described in other reports, but this was the only patient in our series to exhibit pain.

Case 3, Mrs. R.B., age 32 years

This patient was admitted to the labour ward of this hospital at 6 p.m. on 5th September, 1955, in the 40th week of her second pregnancy. The first pregnancy had ended in lower segment Caesarean section for severe foetal distress. It had been decided that this time the patient should undergo trial of labour.

The membranes had ruptured at 5 p.m. on the day of admission, the liquor was clear, the foetal heart sounds were normal, but there were no uterine contractions.

At 10 a.m. on the 6th September the patient developed a temperature of 99·6° F. A vaginal swabbing was taken and penicillin 100,000 units every 8 hours and streptomycin ½ g. every 12 hours was commenced by intramuscular injection. There were no localizing signs, the patient was asymptomatic and appeared well. During the night of 6th–7th September the temperature rose to 101·6° F. and at 4 a.m. on 7th September the foetal heart sounds could no longer be heard. The vaginal swabbing had grown only non-haemolytic streptococci and the penicillin was increased to 1,000,000 units every 4 hours. During the day the temperature remained between 101° F. and 103° F. and the patient looked increasingly ill. Blood cultures were taken during the day but yielded no growth either aerobically or anaerobically.

At 2 a.m. on the 8th September strong labour pains commenced. The temperature was still elevated and the patient looked very ill. An intravenous drip containing 1 g. of Oxytetracycline hydrochloride was set up with instructions to continue in a dosage of 500 mg. every 8 hours. No further penicillin or streptomycin was given. By 6.30 a.m. the cervix was fully dilated. At 6.50 a.m. the foetus was delivered by an easy low forceps under open ether anaesthesia. Immediately on completion of the delivery the patient was cyanosed and the blood pressure was 50/30. There had been no vomiting and there were no abnormal signs in the chest. A diagnosis of acute adrenocortical insufficiency was made and 100 mg. of hydrocortisone free alcohol diluted in 500 ml. of 5 per cent glucose in distilled water was given intravenously. The blood pressure rose to 100/60 but the patient's condition continued to deteriorate, the skin developed a marked cyanosis, and she became noisy and confused. The temperature at 10.15 a.m. was 105° F. At 11.30 a.m. the patient died.

Autopsy. This was performed 3 hours later by Dr. Mary Heseltine. The uterus was normally puerperal. The only abnormal finding in the mother was in the adrenal glands. Macroscopically both adrenals were studded thickly with bright haemorrhages the size of the top of a pin. On incising the adrenals these haemorrhages could be seen throughout the substance. Microscopically extensive haemorrhages were seen involving both the cortex and medulla. In the majority of these areas the tissues were disorganized. The pituitary was macroscopically and microscopically normal.

The foetus showed maceration. The lungs were grey and soft and microscopically showed collections of bacteria, both cocci and bacilli in some of the alveoli. There was no evidence of polymorphonuclear reaction in the lungs. In the cord there was a very marked polymorphonuclear reaction. The foetal adrenal cortex appeared normal.

Comment

The precipitation by the added stress of an anaesthetic and instrumental delivery of the syndrome of cyanosis and low blood pressure without pallor, in a patient already seriously ill

with a severe infection, suggested a clinical diagnosis of adreno-cortical insufficiency. The pressor response to hydrocortisone confirmed this. It is felt however in this case that the adrenal insufficiency precipitated rather than caused death as the patient was very ill indeed with sepsis.

Case 4, Mrs. B.B., age 61 years

This patient was a routine admission to the gynaecological wards of this hospital on the afternoon of 9th May, 1956. She was to have an elective laparotomy to exclude carcinoma of the ovary on the following day. The blood pressure was 160/110 and the haemoglobin 12·6 g. per cent.

The operation was commenced at 9.30 a.m. on 10th May, the anaesthetic being pentothal/tubarine/nitrous oxide/ether. The operation performed was total hysterectomy, double salpingo-oöphorectomy, the pelvic mass having been found to be myomata.

On return to the ward at 11 a.m. the patient was not yet conscious. Her condition appeared satisfactory except for slight cyanosis of the lips. Her skin was warm and dry. The respirations were regular and the heart rate 82 per minute. The blood pressure however was only 50/30. An initial injection of methedrine had no effect on the blood pressure, but a further injection of 15 mg. intravenously and 15 mg. intramuscularly temporarily increased the blood pressure to 80/50. At 11.20 a.m. a further 30 mg. of methedrine intravenously caused an evanescent further rise, but by 11.45 a.m. the blood pressure had again dropped. The patient was still not conscious but her general appearance and condition was satisfactory. A direct eosinophil count was done, showing 150 eosinophils per c.mm.

At 12.45 p.m. an intravenous drip of 100 mg. of hydrocortisone free alcohol in 500 ml. of 5 per cent glucose in distilled water was set up running at 30 drops per minute. By 1.15 p.m. the blood pressure was 130/90 and the patient was becoming conscious. At 4 p.m. the blood pressure was 160/100 and she was fully conscious. A direct eosinophil count was now 19 per c.mm. The drip was continued until 6 p.m. when the blood pressure was stable at 160/110.

Cortisone acetate 25 mg. was given orally and a further 25 mg. by intramuscular injection. On 11th May the blood pressure was maintained at 160/110 throughout the day. The patient was well. Cortisone acetate 25 mg. was given intramuscularly at 8-hourly intervals throughout the day. At 11 a.m. the direct eosinophil count was 25 per c.mm.

The cortisone was continued in diminishing dosage until the 13th May when it was suspended. The patient continued to be quite well apart from a mild pyrexia that responded to penicillin and streptomycin.

Comment

Again this patient presented a clinical picture of good initial general appearance apart from slight cyanosis and a very low blood pressure unrelated to blood loss. The direct eosinophil count of 150 per c.mm. confirmed the diagnosis.

Two of these 4 patients died. It is felt that with earlier diagnosis and more vigorous treatment the first case could have been saved.

Discussion

Acute adreno-cortical insufficiency may result from an absolute or relative lack of adreno-cortical hormones. The normal adrenal response to any stress is mediated through the anterior pituitary by increased production of A.C.T.H. The fact that this normal increase in A.C.T.H. production can be blocked by the administration of cortisone indicates the mechanism of this increase. The greater the stressor agent then the greater must be the dose of cortisone to inhibit this response (Sayers and Sayers, 1947). It would appear that adreno-cortical failure may result theoretically under the following circumstances: failure of the pituitary to produce A.C.T.H., as in the hypophysectomized animal or in Simmonds's disease, from inability of the atrophied or diseased adrenal cortex to respond to this increased production of A.C.T.H., or from prolonged or severe stimulation of the cortex resulting in adrenal exhaustion. Selye (1950) has drawn an analogy between the latter group and the experimental production of diabetes after damaging the islet cells with diabetogenic pituitary extracts.

Adrenal failure in the presence of a diseased cortex is a concept easy to understand as such a gland will show poor or absent response to A.C.T.H. Indeed the very diagnosis of Addison's disease may often depend on this lack of response.

In the apparently normal individual the mechanisms leading to adreno-cortical insufficiency are more difficult to elucidate. Sayers and Sayers (1949) and Selye (1950) trace the development of the changes from the normal resting gland. A sudden intense stress will cause rapid depletion of the sudanophilic substances, ascorbic acid and cholesterol. This type of response is produced by an acute non-fatal haemorrhage, a short-acting bout of exercise or a single injection of A.C.T.H. In the event of a severe acute stress, some of the cortical cells

may undergo partial or complete cytolysis with the formation of lumina or pseudo-tubules. Involvement of the vascular endothelia in this process can open communications between the cortical sinuses and the lumina and diffuse infarction of the cortex may result.

In a slowly developing and constant stress there is a general increase in the size of the gland and the concentration of sudanophilic substances, ascorbic acid and cholesterol is not changed. It is apparent that new secretory units can be constructed at a rate sufficient to meet the increasing demands. It is in this type of gland already adapted to meet a stress that a further sudden stress is likely to produce intense cytolysis and haemorrhagic infarction.

Pregnancy has been commonly accepted as an example of a slowly developing stress with subsequent hypertrophy of the adrenal cortex. Increase in the urinary excretion of corticoids and neutral reducing lipoids has been described by Venning and Browne (1949) and increase in the blood 17-hydroxycorticosteroids during pregnancy has been demonstrated by Gemzell (1953) and Bayliss *et al.* (1955). In pre-eclampsia and eclampsia the levels may be even higher.

The source of this increased corticoid level in pregnancy has been disputed. It is usually stated that the adrenal is normally hypertrophied in pregnancy. Davis and Plotz (1956) however point out that the report of adrenal hypertrophy in pregnancy is based on post-mortem material. Most of the patients from whom the material was obtained died from sepsis or other conditions that in themselves would cause adrenal hypertrophy. They conclude that there is insufficient evidence to state that there are morphological changes in the adrenal cortex in normal pregnancy and suggest that any changes may be qualitative rather than quantitative.

In the pregnant Addisonian the excretion of corticoid-like products may reach that of a normal individual in the last trimester (Jailer and Knowlton, 1950). The foetal adrenal and the placenta have been invoked as sources of these hormones. However, the amount of urinary excretion in the newborn infant is insufficient to support the former hypothesis. Hills *et al.* (1954) have challenged the conclusion that the placenta is the source of this increased hormone and also challenge the fact that the observed increase in urinary 17-ketosteroids is due to adreno-cortical-like substances. The Zimmermann reaction employed for the estimation of 17-ketosteroids will also give positive reactions with 3- and 20-ketosteroids such as pregnanolone. However Jailer and Knowlton (1950) also observe this increase using the antimony trichloride method of assay, which would exclude this possible source of error. Hills *et al.* also suggest that the increased levels of 17-hydroxycorticosteroids in pregnancy may be due to abnormal hepatic metabolism, the ensuing longer survival of the substance causing increased concentration.

Cohen and Kleinberg (1952) have found greater concentrations of A.C.T.H. in the placenta than could be accounted for by the blood content, but this may mean storage rather than production. Bayliss *et al.* (1955) also suggest that the placenta may provide some of the A.C.T.H. stimulation necessary for the adrenal hypertrophy that is usually accepted as a normal accompaniment of pregnancy. A difficulty associated with accepting the placenta as a significant source of adreno-cortical-like hormones is that the increased levels associated with pregnancy do not return to normal for 6–8 days, whereas injected labelled hydrocortisone has a urinary half life of only 3–5 hours.

Tatum and Mulé (1956) studied a series of toxaemic patients in whom circulatory failure developed without apparent fluid loss. They found in this group of patients an electrolyte pattern similar to that seen in Addison's disease. In one case where the serum-electrolytes were estimated both before and after confinement, the drop in serum-sodium did not occur until after confinement. The recorded cases of this type have occurred after delivery or foetal death *in utero*, suggesting that deprivation of some foetal or placental factor is responsible. It is also of interest that these workers found a greater incidence of this collapse after Caesarean section and forceps delivery than after normal confinement. Both of the former two would impose a greater stress on the subject than the latter.

It seems reasonable to conclude that there is

increased adreno-cortical-like function in pregnancy, but the contribution towards this hyperfunction by the maternal adrenal, the placenta and the foetus remains to be precisely determined.

Considering these facts it appears likely that multiple factors may cause adrenal failure acting via a final common path. Either the adrenal may be destroyed by disease such as tuberculosis or trauma and be incapable of producing increased corticoid excretion, or else a wide variety of stressor agents may cause exhaustive over-stimulation of the adrenal by A.C.T.H. In pregnancy the possibility that withdrawal of placental and/or foetal contributions after death *in utero* or delivery may lead to a relative insufficiency of adreno-cortical-like substance must also be considered. Any of these mechanisms could produce an absolute or relative lack of cortical hormones.

How does this lack of cortical hormones produce the clinical picture obtained?

There appear to be at least two distinct syndromes of acute adreno-cortical insufficiency. The first of these is presented by the patient with Addison's disease on passing into crisis, or the adrenalectomized animal in whom no substitution therapy is given. The outstanding feature of these cases is the electrolyte and metabolic disturbances characterized by increased urinary excretion of sodium, diminished excretion of potassium, hypoglycaemia, diminution in the extracellular fluid volume with shock occurring secondarily to this hypovolaemia and hyponatraemia. In a protected environment the disturbance of electrolyte metabolism is the major cause of death in adreno-cortical failure. All these features can be explained on the known functions of hydrocortisone and aldosterone, particularly the latter. Mach and Fabre (1955) have shown that aldosterone will correct the glucose tolerance in Addison's disease as well as the disturbed electrolyte pattern.

The second and even more dramatic group are those in whom cortical failure is announced by a sudden fall in the blood pressure as in the 4 cases described in this paper. Abdominal pain was an additional feature in one of these cases, and has been in many of those previously described but by no means all. The high eosinophil count associated with the adrenal insufficiency would be expected from the known role of the adrenal cortex in controlling lymphoid and eosinophil response. But the most striking feature is the profound hypotension, unaccompanied initially by the signs that accompany and distinguish haemorrhagic and traumatic shock. The patient is initially warm and well orientated, cyanosis is almost invariably present, and there is not the profound anxiety that accompanies shock from blood loss. With the passage of time these features will develop, but initially, when it is so important to recognize the difference, they are absent.

It is apparent that the hypotension which is the outstanding feature of these cases has a different pathogenesis to that occurring secondarily to fluid and electrolyte changes, as evidenced by the first group. The suddenness of this shock is referred to by Gaunt and Eversole (1949). That this shock can occur in the presence of a normal electrolyte pattern is shown by Ingle (1942). Ingle goes on to add: "The observation that the cortin treated adrenalectomized dog can recover without the administration of either fluid and electrolytes is important . . . It is difficult to explain the known lowered resistance of the adrenalectomized animals to stress in terms of the known effects of cortical principles on salt and water metabolism and on carbohydrate metabolism. Adrenal shock may occur without sodium loss by the kidneys and without hypoglycaemia."

Part of this protective mechanism against infective stress is demonstrated by the limited ability of the adrenalectomized animal to form gamma globulins in the presence of infection as compared with the normal (Lewis and Page, 1949). But the onset of sudden shock would appear to demand the withdrawal of some specific effect that adreno-cortical hormones normally exert on the vasculature.

It is now accepted that the presence of adrenal cortical tissue is essential for the development of renoprival hypertension. Floyer (1955) suggests that the healthy kidney maintains the blood pressure within normal limits by inhibiting the extra-renal pressor mechanism. These facts suggest that the extra-renal pressor substance is produced in the adrenal cortex, or requires

the presence of functional cortical tissue for its production elsewhere.

In 1938, Swingle *et al.* showed that the absence of adreno-cortical hormones causes generalized capillary atony, dilatation and stasis resulting in increased capillary permeability. Two significant contributions by Ramey, Goldstein and Levine (1951) and Fritz and Levine (1951) have helped to clarify this. These workers showed that in the adrenalectomized dog exercise leads to a progressive fall in the blood pressure and the animal dies in shock. Post-mortem shows splanchnic engorgement. In the normal animal splanchnic vasoconstriction occurs in response to exercise and the blood pressure is maintained. They also showed that the sensitivity of the adrenalectomized dog to noradrenalin was substantially lower than normal, and that even this limited initial response is lost with succeeding injections of noradrenalin. The capillary responsiveness of the adrenalectomized animal can be restored by injection of adrenal extracts. They conclude that the absence of splanchnic vasoconstriction in the working or stressed adrenalectomized animal is a result of diminished sensitivity of the small vessels of this area to endogenous noradrenalin.

Similar changes can be demonstrated in the rat meso-appendix preparation. It was also demonstrated that repeated applications of noradrenalin in the adrenalectomized rat cause actual vascular damage, with the escape of red cells through the vessel wall. These changes can be reversed by the injection of cortical hormones or more rapidly by their local application.

The conclusion reached is that cortical steroids are necessary to allow blood vessels to respond regularly and repeatedly to minute quantities of noradrenalin and at the same time to prevent the toxic effects upon the vessels of large quantities of exogenous noradrenalin.

It is of importance that some initial vasoconstriction to noradrenalin will occur in the absence of adrenal steroids. Vogt (1955) points out that the evidence suggests that the role of corticoids in this function is permissive rather than initiating, as would be expected from its other functions (Ingle, 1949; Engle, 1953; Mason, 1955). Vogt states: "The corticoids bestow on the tissues the capacity to react efficiently to internal or environmental stimuli, but are not in themselves those stimuli. The loss of reactivity of at least some tissue to adrenalin and noradrenalin would fit that conception."

With these facts in mind a working hypothesis of the pathogenesis of acute adreno-cortical insufficiency may be advanced.

An adrenalectomized subject, or an Addisonian in a protected environment, that is, not exposed to a severe stress, will primarily show the effects of hypocorticism in the electrolyte and body fluid pattern and carbohydrate metabolism. In the resting state the blood pressure will be low because of the secondary hypovolaemia, and shock levels of blood pressure will not be reached until further significant changes have occurred in the electrolytes and fluids.

In a similar subject exposed to a more severe stress, the permissive and protective functions of the adrenal steroids on the small vessels necessary for haemostasis are lacking and generalized vasodilatation and shock will occur.

In a previously normal subject exposed to a very severe stress, or exposed to a further stress when already adapted to an existing stress, exhaustive over-stimulation of the cortex will result in a sudden diminution in the output of corticoids, so that the resulting lack may be relative rather than absolute. This lack of corticoids in a subject under stress results in ultimate failure of the arterioles and metarterioles to respond to endogenous or exogenous noradrenalin with consequential gross expansion of the vascular bed and fall in blood pressure. After this hypotension has existed for a time the production of vaso-active ferritin would also play a part in arteriolar unresponsiveness. It is because of this initial vasodilatation and slow peripheral circulation that the skin of these people is initially warm and cyanosed, in marked contrast to the cold pale skin of a subject in the hyper-reactive phase of haemorhagic or traumatic shock.

Summary

(1) The aetiology of acute adreno-cortical insufficiency is discussed. The syndrome may occur in previously normal individuals or in those with known or unsuspected hypocorticism.

The importance of the increasing use of cortisone in producing hypocorticism is discussed.

(2) The histopathology and histochemistry of the adrenal cortex in these cases is briefly described.

(3) Four cases of acute adreno-cortical insufficiency are reported. Two of these followed routine gynaecological operations; both of these cases survived. Two occurred in pregnancy, one following elective Caesarean section for diabetes mellitus and one following a severe intra-partum infection. Both of these patients died. The clinical features common to all of these cases are described.

(4) The role of the maternal adrenal, the placenta and the foetal adrenal in producing evidence of apparent hypercorticism in pregnancy is discussed, and the bearing that these factors may have on the development of adreno-cortical insufficiency in pregnancy is considered.

(5) Attention is drawn to the two differing forms of adreno-cortical insufficiency; the first characterized by changes in body fluids and electrolytes, with hypotension and shock developing secondarily to these changes; the second based on the withdrawal of a specific permissive role of adrenal steroids in maintaining arteriolar responsiveness in states of stress.

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URINARY FISTULAE IN WOMEN*

BY

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HISTORICAL

FISTULOUS communications between the genital apparatus and the adjacent urinary tract are among the most troublesome and deplorable diseases women are liable to suffer from. There can be no doubt that these infirmities existed from time immemorial. An extensive urinary fistula was found by Professor Derry (1935) of Cairo in the mummy, or more correctly, the dried-up body of a woman called Henhenit, who was one of six ladies in the court of Mentuhotep, of the eleventh dynasty, who reigned in Egypt about 2050 B.C. The pelvis of this woman is dolicopellic and considerably contracted in its transverse diameter. In Figure 1 which represents the anterior surface of the mummy you can see: (1) the enormously dilated bladder, (2) the thickened infected lining of the bladder, and (3) a large vesico-vaginal fistula. When I examined this mummy myself I found an extensive complete tear of perineum. This finding supported the deduction that the fistula was the result of difficult labour. In Figure 2 you can see the tear in the perineum. The line of junction of the skin with the granulating surface of the tear can be distinguished by the difference in colour between the brown skin and the bluish granulating area. I have cut sections from the edge of the perineal tear near the rectal side for microscopical examination. In Figures 3 and 4 we see: (1) a vessel, (2) vacuolated fibrous tissue and (3) muscular tissue. It is most unusual to find such preservation of tissues four thousand years after the death of the subject. Apart from the accidental discovery of this urinary fistula in the mummy of Henhenit no mention of this infirmity is found in books on ancient medicine.

It is indeed surprising that a lesion so palpable, with symptoms so obtrusive as urinary fistulae, should pass unnoticed by all Greek and Roman writers. The first mention I came across was in *Al-Kanoon*, the celebrated work of Avicenna, the Persian physician whose millennium was celebrated in Teheran 5 years ago. This careful observer says in the chapter on "Contraceptives" that measures to prevent pregnancy should be adopted by girls who get married too young. Their labours, he adds, are often difficult and may be followed by incontinence of urine. Reference to fistula was also made by him in the chapter devoted to vaginal atresia. In this chapter he describes an operation for the treatment of this lesion which consists of dissecting a passage between the bladder and rectum, and warns the surgeon to take the greatest care in avoiding injury of the bladder while making this dissection, lest the patient might have incontinence of urine from which she has not the slightest chance of ever being cured. The first reference in European literature to this infirmity was made by Platter in 1597; but nothing was suggested by him in the way of treatment. During the next hundred years several clear descriptions of urinary fistulae following difficult labours appeared and surgeons diligently attempted to cure them by surgical operations. Their attempts entirely failed. In spite of their failures they still carried on, with never flagging patience trying new methods, when one by one the older methods proved themselves useless. But it was only in 1663 that the first glimpse of hope appeared, when Van Roonhuyse of Amsterdam proposed to close fistulae by denudation of tissues and suture. He might have had an occasional success, but it was Fatio who published in 1752 the details of 2 successful operations that he had performed many years before. He placed his patients in the lithotomy position, and exposed the fistula with a speculum. He then refreshed the edges with a

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delicate pair of scissors, and brought them together by passing sharpened quills through them and winding a thread over the ends of the quills.

Eighty-two years later (1834) Jobert de Lamballe planned and put into execution an operation which consisted in pulling the cervix down by traction. This was followed by a broad denudation of the edges of the fistula, and an exact approximation of the edges by interrupted sutures. In difficult cases he advised making wide incisions in the lateral vaginal walls, in order to relieve tension on the sutures. In cases in which he found the cervix densely implicated in scar tissue he advised liberating it from the bladder by making a transverse incision in the vault of the vagina. He called this procedure "Opération par Glissement". Jobert de Lamballe had a few successful cases by using this method; but his followers, attributing the success of his method to the sliding of the flaps, failed entirely to grasp the value of wide denudation of the edges of the fistula. In their hands the operation was a complete failure. In 1841 Ryan of the Metropolitan Free Hospital in London claimed many successes by nursing patients who developed fistulae after labour on their face or side, tying a catheter in the bladder and plugging the vagina with oiled lint. Cure of fistulae by operation was at that period considered hopeless, so much so, that Frederick Dieffenbach, a great master of plastic surgery, wrote in his book on operative surgery published in 1845: "It is with shame that we must still acknowledge that the lucky cure of a vesico-vaginal fistula must be always reckoned among the rarest occurrences."

This state of pessimism did not last long, as 7 years later (1852) Sims of Alabama devised and published a technique in which he denuded the edges of the fistula in a funnel-form down to, but not including, the vesical mucosa and suturing the edges of the fistula by silver-wire sutures which he applied at suitable intervals, and secured with clamps consisting of 2 parallel bars. He obtained, by following this method, 230 cures in 312 patients. This was a truly marvellous achievement considering that most of his early cases were done in the pre-anaesthetic pre-antiseptic days. In 1858 Bozeman, a young American surgeon, a pupil and disciple of Marion Sims, came to Paris and successfully operated on a large number of fistulae in different hospitals, placing his patients in the Sims' semi-prone position and using the duckbill speculum invented by his master. He used a head-mirror to reflect light on the field of operation. Sims himself paid a visit to Paris 3 years later and demonstrated his technique which was greatly admired by French surgeons. He attributed his success to the wide denudation of the edges and the use of silver-wire sutures and constant drainage of the bladder by a catheter tied in the urethra. The use of silver-wire was undoubtedly a great improvement on unsterilized silk which was used at that time; but it was not an innovation with Sims. Luke of Charing Cross used it in closing fistulae in 1850; but Sims has the credit of popularizing its use in America and elsewhere. In Great Britain, according to Pozzi and Jayle, two contemporaries of Sims, Baker Brown and Simpson, were obtaining successes, in London and Edinburgh, in the treatment of fistulae using silver-wire and devising several new instruments.

After his visit to Paris Sims went to London, where he had a grand reception. An account of this visit is given by McKay (1922) in his book *Lawson Tait, His Life and Work*. It runs as follows:

"About Marion Sims, Tait spoke frequently, and always with admiration. He considered that as far as America was concerned Sims was the father of gynaecology there, if not the father of modern gynaecology. Tait mentioned to me that the first time he met Sims was at one of the annual meetings of the British Medical Association. He was sitting on a bench waiting for the meeting to open, when he heard a man with a very pronounced Yankee accent say: 'There is one man I have come here to meet, a young fellow called Lawson Tait: I want to have a talk with this young fellow.' Tait introduced himself and became, ever since, a life-long friend of Sims. Tait also related to me that, in a conversation he had with Sims, he alluded to Sir Henry Thompson's operation on the French Emperor as being one of the best instances of bad luck that he could remember, Sims, in

answer said 'I'll tell you another instance almost as bad. During my visit to London I was asked to perform an operation on a case of vesico-vaginal fistula at the Samaritan Hospital. The case was a difficult one, but the operation was in every way satisfactorily performed. The patient, however, died six days later and a post-mortem revealed the fact that I had closed both ureters with the sutures. I performed the same operation hundreds of times in America and yet this was my first death.'" One of the most important contributions of Sims's work on fistulae is found in a book of 250 pages published in 1868 by Emmet, Sims's most distinguished pupil, who, according to Howard Kelly, acquired greater technical skill than Sims and added to his technique many important additions of his own. Sims himself who was excessively occupied and travelling from one place to another kept few or no records of his work. Without Emmet many of the most important details necessary for the success of the operation would never have been brought to the world.

Shortly after the publication of Emmet's book two general surgeons at Kasr el-Ainy Hospital in Cairo, Dorry Pasha and, at a later date, Herbert Milton were getting great success in the treatment of urinary fistulae using Sims's method and a dedoublement technique developed locally. Herbert Milton published his cases in *St. Thomas's Hospital Reports* and described a new method for the treatment of wide destruction of the base of the bladder by transplantation of flaps taken from the vulva. Unfortunately Dorry Pasha did not publish his results but you will see in the film which will be projected after the lecture the box of instruments which he used in operating on fistulae.

For many years Sims's method remained the operation of choice; but gradually it began to show unmistakable signs of falling into disuse, owing to the advent of better methods. In spite of this it still has great admirers, foremost of whom is Chassar Moir of Oxford, who in 1954 published a series of 100 consecutive cases of fistulae in which he obtained, by a modified Sims's method, a 100 per cent cure. This method undoubtedly gives very good results in suitable cases in the hands of experienced surgeons, but the consensus of opinion nowadays is in favour of the flap-splitting operation originated by Martin (1879) and Sänger (1888) and developed by Mackenrodt (1890–91). This operation consists in detaching the bladder on all sides from the vagina, and sewing the bladder flaps and the vaginal flaps independently to each other. A prototype of this operation was published by Maurice Henry Collis in 1861, almost thirty years before Sänger and Mackenrodt published their method. To do Collis justice I shall publish the following extract from his paper in which he describes the details, and emphasizes the merits of the procedure over Sims's operation which was then in vogue.

"The operation," (he says) "consists first in splitting the margin of the fistula all round, so as to separate the vesico-vaginal septum in two equal portions, one half consisting of the vaginal mucous membrane and submucous tissue, the muscular portion of the septum being equally divided between the two. Anyone (he goes on to say) who has removed a ring of mucous membrane from ever so small a fistula will have observed how large it becomes under the process, and sooner or later will have probable cause to regret the loss of substance thus entailed; whereas, in my operation, if it fails, it leaves the patient in no worse condition for subsequent treatment than before. Moreover, in large gaps, where the loss of substance is to be measured by square inches, no person could expect union by simply paring the edges and drawing them together by interrupted sutures. The strain on the threads would be too great, and they would inevitably cut out."

It is remarkable that Collis's method is not to be found described in any of the English, French, German or American textbooks, except that of Lawson Tait, published in 1889. Lawson Tait adopted and popularized Collis's method and seems to have had great success with it. The following whimsical passage quoted from his book *Diseases of Women and Abdominal Surgery* gives you an idea of the frequency of urinary fistulae in his days. It runs as follows:

"I have already said that operations for vaginal fistulae are rarely paid for, except in gratitude, because the patients are nearly always poor. I must have operated on two or three

hundred cases, and I have not yet been remunerated to an extent which would pay for the instruments I have bought for the purpose."

In spite of Sims's successes the gloomy prospect of curing a fistula by vaginal operation prevailed. In 1872 Sir James Young Simpson said in his book *Clinical Lectures on the Diseases of Women:* "A urinary fistula is an infirmity which is beyond all relief and all hope." It is this atmosphere of pessimism that encouraged surgeons to try some way of approach other than the vaginal, to cure these fistulae.

In 1890 Trendelenburg made a radical departure from all the foregoing methods by opening the bladder suprapubically and extraperitoneally, freeing the bladder wall around the fistula and closing the defect with catgut. von Dittel in 1893 opened the peritoneal cavity, detached the bladder from the uterus, and closed the fistula by catgut.

These techniques did not appeal much to gynaecologists but genito-urinary surgeons find them suitable for all forms of vesico-vaginal fistulae.

The year 1894 showed a great advance in the operative technique for the cure of fistulae, when Mackenrodt published the flap-splitting technique which bears his name. All later techniques are simply modifications of Mackenrodt's operation adopted to suit the different types of fistula.

Aetiology

The majority of urinary fistulae in Egypt are the result of pressure necrosis following a long and difficult labour.

The process is as follows: When labour becomes difficult on account of disproportion between the pelvis and the presenting part, or when the presentation is abnormal, the uterine contractions increase in strength and endeavour to force the presenting part through the brim. The membranes protrude and premature rupture occurs. The uterus, in such cases, usually passes into a state of tonic contraction. The presenting part is forced against the brim and either gets tightly impacted therein or in the pelvic cavity as the case may be. In cases in which impaction at the brim occurs before full dilatation of the cervix the continued pressure on the insufficiently effaced and undilated cervix, as well as on the vault of the vagina and the bladder, will cause necrosis and ultimately sloughing of these tissues and the formation of a fistula that may implicate the cervix, bladder and ureter. In some of these cases spontaneous healing of the bladder lesion may occur and the ureter alone, on account of the constant dribbling of urine from its orifice, remains open giving rise to a uretero-vaginal fistula.

If the impaction occurs in the pelvic cavity or at the outlet the urethra and base of the bladder as well as the trigone will be lying in the direct plane of compression. In these cases vesico-vaginal and urethro-vaginal fistulae may occur. If compression of the presenting part occurs at the outlet and lasts for a long time the entire urethra may slough away. In grossly neglected cases the whole vagina may slough away and be replaced by a narrow slit surrounded by scar tissue and pervaded by fistulous tracts. Diverticula may be formed in the vault of the vagina or inside the bladder where the urine stagnates and leads to the formation of stones.

The process just described accounts for the majority of fistulae which occur as a result of labour, but fistulae following labour can also occur from direct injury during the operative procedures used for delivery. The perforator may slip and go through the vesico-vaginal septum, or the forceps may cut through the septum if the vagina tightly embraces the head of the foetus. The vaginal vault and cervix may also get nipped by a blade of the forceps or cranioclast if wrongly applied and give rise to extensive bladder and ureteral injuries.

These complicated cases have formed the bulk of patients on whom I had to operate during the last fifty years. Before 1919 the overwhelming number of fistulae met with in Egypt was a sequel of neglected labour. The number of cases was so great that I devoted a ward of 10 beds to urinary and faecal fistulae and the beds were always full. Late in 1919 I opened the first antenatal clinic and extern maternity department in Egypt. In 1920 I opened three more.

Success of this project was overwhelming. Thousands of cases were delivered every year in their own houses by the medical students and

pupil midwives under full supervision. Seven years later the Ministry of Health was encouraged to open centres in different parts of the country. The number of patients delivered in these centres in 1955 amounted to a quarter of a million.

In countries, like yours, which were ahead of us in adopting expert obstetrical services, the number of fistulae due to faulty obstetrics has fallen considerably, but unfortunately this decrease in number has been almost balanced by a higher incidence of cases due to surgical operations. American and European literature teems with reports on accidental injuries to the ureters and bladder as a sequel to surgical operations. In Chassar Moir's (1954) article on 100 cases of fistula previously referred to 36 cases only resulted from obstetrical causes, while the gynaecological group accounted for 64. The operative procedures which accounted for the majority of the fistulae in his series were difficult pelvi-abdominal operations except in 18 cases in which the fistulae followed simple colporrhaphies. Some of these he goes on to say were due to a fault of technique and some arose from trauma inflicted on the upper urethra by unskilful catheterization after colporrhaphy. The sling operation itself which is performed for the cure of stress incontinence of urine was responsible for 3 cases in his series.

The Situation of a Fistula

In fistulae that follow difficult labour the situation depends, as I have said before, upon the plane of compression of the presenting part as well as the degree of dilatation of the cervix when this compression occurs. In this connexion I wish to point out that there is a misconception about the possibility of involvement of the ureters in the sloughing process that leads to the formation of fistulae. It used to be taught that, owing to their displacement above the brim, the ureters, in protracted labour, do not share in the compression that leads to the formation of fistulae, but are involved as the result of infection spreading to the wall of the ureter from sloughs in the vault of the vagina.

That this is not so is seen in Figure 5 which represents one of ten dissections I performed on the bodies of women who died undelivered as a result of rupture of the uterus during labour. The trigone of the bladder, the internal openings of the ureters, as well as the upper third of the urethra, are within the area of compression. These dissections were also of help to me in clearing up another common misconception about the rarity of urethral fistulae in cases where the compression occurs in the higher planes of the pelvis. In each of the ten dissections, I found that when the bladder was pulled up it dragged the urethra upwards with it to such an extent that a good part of the latter lay in the area of compression.

Diagnosis

The *diagnosis* of vesico-vaginal fistulae is usually very easy. If the hole is big it can be detected by placing a finger in the vagina and introducing a sound into the bladder through the urethra.

But tiny fistulae usually lie concealed in scar tissue. To detect them we fill the bladder with a coloured solution, and then retract the posterior vaginal wall by a speculum and look for the hole through which dribbling is occurring.

Ureteric fistulae are often difficult to find. In order to detect them we inject the bladder with a coloured solution and watch whether the fluid does or does not leak in the vagina. We can also verify the diagnosis by plugging the vagina with two pieces of gauze which we remove after two hours. If the upper one is found soaked with uncoloured urine, the fistula is evidently ureteric. In difficult cases the cystocope is of help in determining the site of the fistula and the state of the ureteric openings.

Urethral fistulae are often so tiny as to escape notice. To determine their position we place a speculum in the vagina, block the meatus with the thumb, and ask the patient to strain. The fluid will be seen flowing out of the hole.

Before concluding an examination of a case of fistula we should take care not to miss the presence of more than one hole, and should also look for the possibility of the presence of calculi in diverticula in the vagina or bladder. *Associated complications* such as rectal fistulae, para- or peri-metritis, salpingitis and inflammatory lesions of the vagina and perineum should also be noted.

Symptoms

In patients who develop fistulae after labour, incontinence of urine becomes evident soon after delivery if the fistula is traumatic; but if it results from pressure necrosis cystitis first develops but incontinence occurs only when the slough begins to separate. This usually takes 4–7 days. Dribbling of urine in the vagina will be constant if the fistula is vesical or ureteral but in urethral fistula constant dribbling of urine does not occur but some of the urine passes through the hole and unpleasantly splashes the patient's parts during micturition.

The effect of the constant dribbling of urine into the vagina and out on to the vulva, perineum and adjacent tissues will soon show itself. Dermatitis with excoriations both within the vagina and outside it develop. The vulval hair becomes encrusted with salts. The parts involved become exquisitely painful. The effect of this on the general health of the patient soon shows itself. She becomes emaciated and depressed and seeks solitude and evades society on account of the penetrating smell of urine which emanates from her.

Treatment

No attempt should be made to close a fistula until all granulating surfaces are quite healed up and complete involution of the pelvic organs has occurred.

Full investigation of the urinary apparatus by intravenous pyelography and excretory urography should be made as well as a full examination of the urine. A culture should be made and sensitivity to the different antibiotics of any bacteria present should be noted. In difficult and tiny fistulae the orifice of the fistula and the relation of the ureteric orifices to the edges of the fistula should be located by the cystoscope. The best time to operate, provided that the general and local conditions allow it, is at least 3 months after labour. Nature is thereby given ample time to effect a spontaneous cure of the fistula if that were possible. If the operation is delayed too long the edges of the fistula get more sclerosed and the vascularity poorer.

Surgical Treatment

I do not intend to describe the various operative techniques advised, but shall content myself with the technique which has given me the best results.

I shall not describe the transvesical nor the transperitoneal routes for the simple reason that I have been able to tackle almost all my cases—758 besides 210 of which I kept no records—by the vaginal route. The few cases in which I failed to close the fistula from below I also failed to do so when I attempted to close it from above. The cause of failure in both routes was the immobility of the bladder produced by dense infiltrations.

The technique I follow is that of the original flap-splitting operation, with certain modifications necessitated by the nature of the case I would be dealing with. I do not practise the wide separation of the bladder advised by most surgeons who use this method; but only such separation as is sufficient to prevent tension on the sutures when tied. I do not close the bladder wall by more than one tier of sutures. I put my patients in the lithotomy position while operating, and retract the posterior vaginal wall by the ordinary Auvard's speculum. In some cases I also employ lateral specula. I try to get good exposure of the fistulae either by pulling the cervix down by tenaculum forceps if that is possible, or by putting two Little's bladder forceps at a distance of 1 cm. from the edges of the fistula. In cases where the vagina is narrowed by cicatrices I widen the vagina by making lateral incisions. In only a few cases have I had to resort to a Schuchardt's incision. I begin the operation by passing a female metal catheter into the bladder to assure myself of the patency of the urethra. I then push the catheter beyond the fistula in order to use it as a counterpoint and to help me in putting the line of union between the vaginal and bladder walls on stretch. I next make a circular incision starting at a point where I think it more likely to find the line of cleavage and then extend the incision around the fistula. If I come across scar tissue I deliberately remove it by scalpel or small scissors. I then dissect two flaps, an inner consisting of bladder wall or urethra and an outer consisting of vaginal wall. Two short

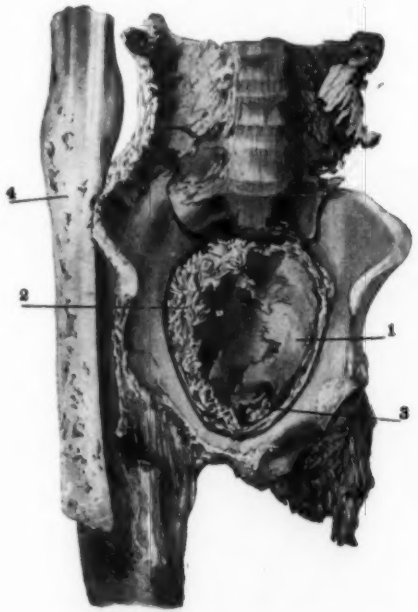


FIG. 1

Mummy of Henhenit, who was either a queen or a dancer in the Court of King Mentuhotep, 2050 B.C., showing a large vesico-vaginal fistula.
(With kind permission of Professor Derry.)
1. Bladder cavity enormously dilated. 2. Thickened and infected lining of bladder. 3. Large vesico-vaginal fistula. 4. Arm of the mummy lying at the side of body.

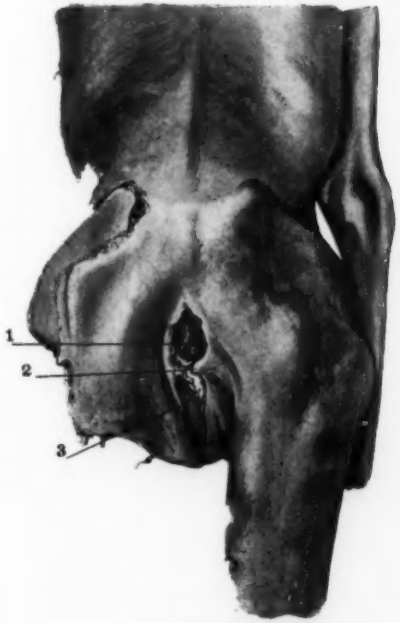
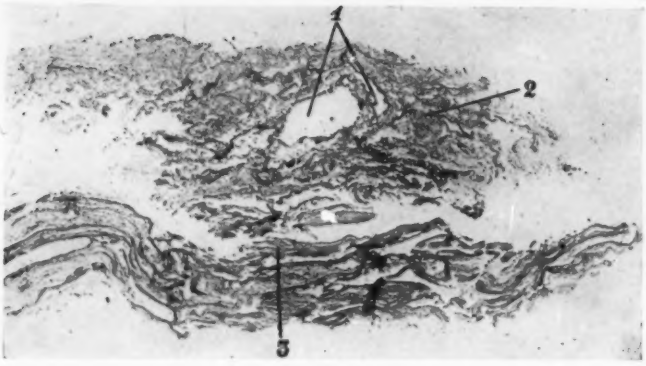


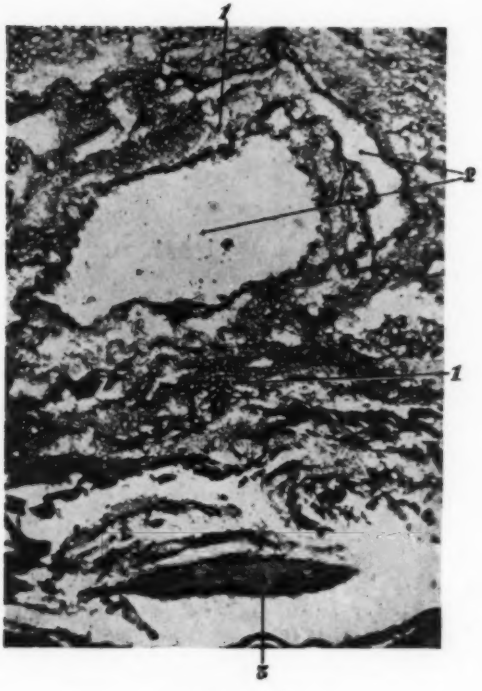
FIG. 2

Posterior surface of the mummy of Henhenit, showing a complete tear in the perineum.
1. Anal opening. 2. Torn perineum. 3. Vagina.



A

FIG. 3



B

FIG. 4

FIGS. 3 AND 4

Sections *A* and *B* taken from the edge of a complete tear of the perineum near its rectal end. (A. Guirgis.)

1. Vessels. 2. Vacuolated fibrous tissue. 3. Muscular tissue.

N.M.

FIG. 5

Anatomical relations of the ureters to the bony pelvis in a case in which rupture of the uterus occurred as a result of obstructed delivery.

(*Specimen 151*)

The specimen was removed post-mortem from a patient who died as a result of difficult labour. The child presented by the head, but owing to pelvic contraction natural delivery was impossible. The lower uterine segment is seen to be greatly distended. The contracted upper uterine segment lies completely above the buttocks. The foetus, in other words, is entirely surrounded by the distended vagina and lower uterine segment.

A vertical tear is seen in the left postero lateral side. The placenta was partially extruded into the peritoneal cavity through this rent. The shoulder and arm of the foetus filled the rent and prevented the occurrence of any appreciable intra-peritoneal haemorrhage.

The trigone of the bladder with the ureteric openings were in the direct plane of compression.

1. Symphysis pubis. 2. Round ligament of uterus. 3. Retraction ring. 4. Placenta. 5. Umbilical cord. 6. Foetal head. 7. Ureter.

N.M.

incisions at either side or one upwards towards the cervix and one downwards towards the meatus may, in some cases, be of use in finding the line of cleavage and may render dissection of the flaps easier. I do not remove a ring of vaginal or bladder wall. This practice is absolutely unnecessary and will, if applied as a routine, jeopardize the chances of cure if the operation has to be repeated. Before closing the bladder I assure myself that there are no stones inside it. For suturing the bladder walls I use No. 0 or No. 1 chromic catgut. The sutures should pass through the muscular wall of the bladder including a good bite of tissue but should neither perforate the wall nor include the bladder mucous membrane. The sutures are passed with small well-curved round-bodied needles and must be introduced with the greatest care and should emerge just at the edge of the mucous membrane of the bladder. If this is done you will ensure a clean straight line inside the bladder when the sutures are tied. The lateral sutures should be passed first. This will help in visualizing a ureteric opening that may be lying near the edge. If one is discovered the wall of the ureter should be dissected from the surrounding connective tissue for a short distance. The suture in such a case should be passed first in the muscular wall of the anterior flap of the bladder and then in the anterior wall of the ureter at a short distance from the orifice and lastly in the muscular wall of the posterior bladder flap. When a suture placed in this manner is tied the ureteric opening will look inwards towards the bladder cavity and the ureteric wall will be neither occluded nor compressed. When all the bladder sutures have been tied we should test the impermeability of the bladder by filling it with a coloured solution. If leakage occurs I presume that there is a fault with the suturing or that a tiny fistula may be lying embedded in scar tissue to which I should attend. Haemostasis should be perfect. The vaginal flaps should be sutured in whatever plane will cause less tension on the flaps when the sutures are tied. Here and there a suture may be made to catch the underlying bladder in order to prevent any dead space. I habitually use silkworm gut for the vaginal sutures. In some of my later cases I employed No. 1, 30 days, chromic catgut or nylon sutures and found them reliable.

After closure of the vaginal flaps I wash the bladder cavity again and leave a catheter tied in the urethra for 10–12 days. With the introduction of the sulpha compounds and antibiotics and the use of a buchu and hyoscyamus mixture during convalescence we have ceased to get blockage of the catheter by deposition of salts inside or around it. During convalescence the patients are at liberty to lie on their backs or sides. We allow them free movement in bed. It is immaterial whether a suction apparatus is or is not used. We remove the sutures on the 17th day. If they are left longer they will cut through the mucous membrane of the vagina and the knots may become embedded. In removing such a knot, we pull on one end of the suture only. The knot will then become visible. In cutting the knot care should be taken not to cut both sides of the suture above the knot. If we do a piece of silkworm will be left behind, nor should we cut the two sides of the suture below the knot and leave the knot behind, else it will cause trouble to the patient and to her husband who may sue the surgeon for damages. Before discharge from the hospital the patient is instructed to avoid marital relations for 2 months.

Several modifications of the flap splitting operation have to be occasionally adopted in order to suit particular cases but the principle is always the same.

In a type of fistula we sometimes meet with in Egypt, the trigone and the neck of the bladder, as well as the upper third of the urethra, are entirely destroyed. The remaining part of the urethra is blocked, and is separated from the bladder by dense scar tissue. Such cases offer great technical difficulties and indeed were considered inoperable. I have, however, been able to cure most of them by the technique shown in Figures 6, 7 and 8. I begin the operation by perforating the blind end of the urethra, I then liberate its wall by careful dissection from the surrounding tissues. I next remove the scar tissue that intervenes between the urethra and the opening in the bladder. The next step is to mobilize the bladder by dissection which in some cases has to be carried as far as the peritoneum. When that is done I suture the edges of the

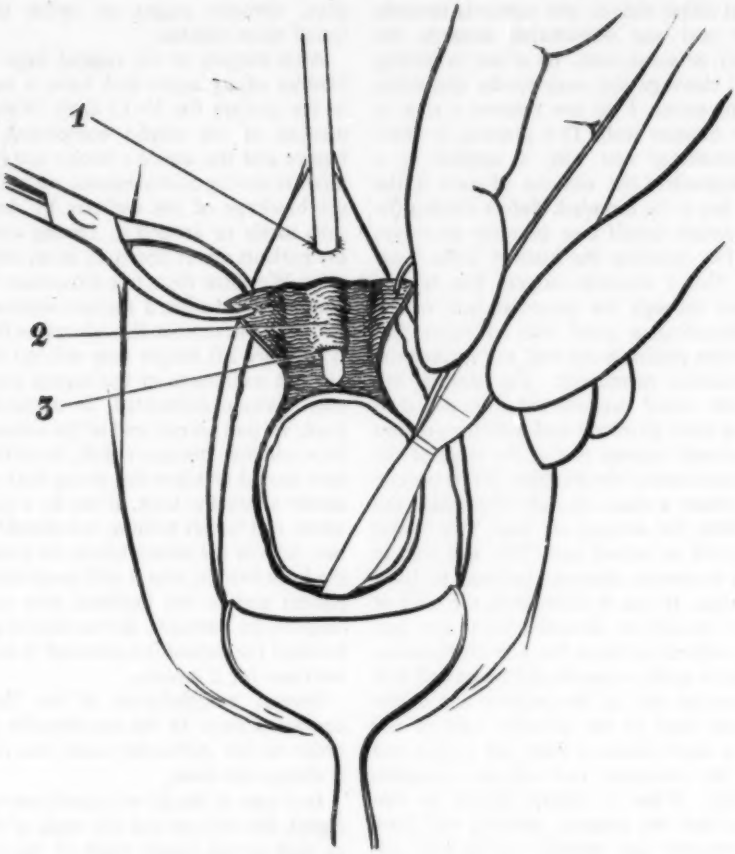


FIG. 6

Vesico-urethral anastomosis.
First step. The scar tissue has been removed.
1. Probe placed in urethra. 2. Denuded wall of urethra. 3. Tip of probe.

bladder together, leaving a small gap in the centre which I use in making an anastomosis between the bladder and urethra.

Another type of fistula which I sometimes meet with is the "vesico-isthmial" the so-called vesico-uterine. In dealing with this type I make a transverse incision in the vault of vagina and dissect the bladder off the cervix. When I reach the level of the fistula I stop dissection and divide the cervix in the middle line up to the site of the fistula. I find that this greatly facilitates further dissection and suturing of the flaps.

Another rare type of fistulae is the uretero-vaginal. The treatment of this type depends upon the amount of scarring present at the vault. If that is not great I begin by dissecting the ureter vaginally for a short distance. If that has been satisfactorily completed I dissect the vaginal wall off the bladder and mobilize it to the extent I find necessary to approximate it to

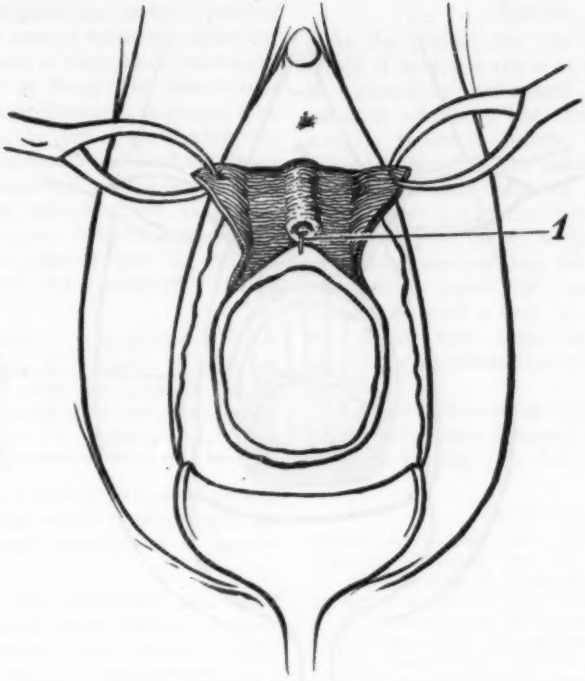


FIG. 7

Vesico-urethral anastomosis.
Second step. The upper wall of the bladder is dissected out and sutured to the roof of the urethra.
1. Suture uniting urethra with bladder.

the ureter without tension. I then implant the ureter in the bladder through an opening which I make for the purpose. I do not use ureteral catheters. I have done this successfully in 10 cases. In 4 other cases I failed to make the implantation to my satisfaction and had to adopt the abdominal route. After all successful operations on fistulae the patient gets complete control over micturition irrespective of the site or the size of the fistula, except in the fistulae in which the trigone and neck of bladder have been destroyed. A certain number of these patients will have continence while lying down but the moment they get up the urine begins to dribble, in spite of the fact that the bladder neck had been buttressed with all available tissue and to all appearances the fistula was successfully closed.

To remedy this defect the sling operations which were devised for the cure of stress incontinence have been adopted. Foremost amongst these is Aldridge's (1942) modification of the Goebell Stockel technique. In this operation strips of fascia of the oblique muscles of the anterior abdominal wall are made and pulled down by a forceps pushed through an incision made in the vagina. The strips are then sutured under the urethra so as to form a sort of supporting sling. The results are not always satisfactory on account of the difficulty in deciding upon the amount of tension necessary to support the urethra. It is sometimes too much and sometimes too little.

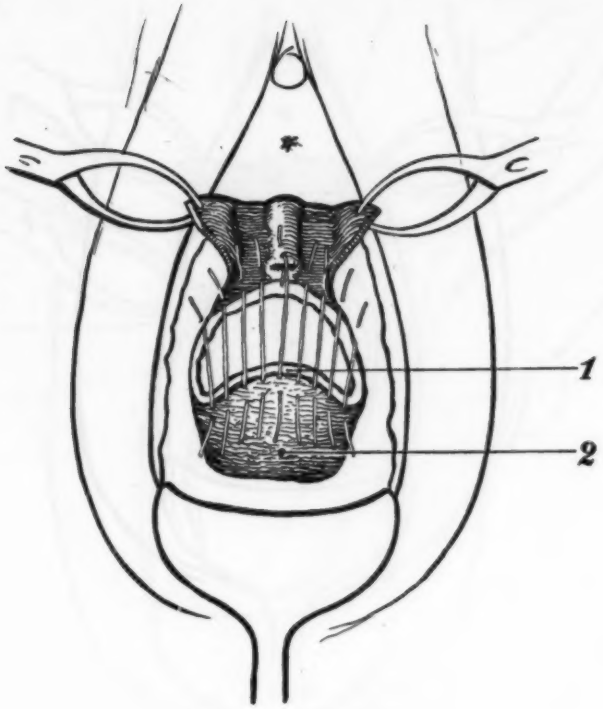


FIG. 8

Vesico-urethral anastomosis.
Third step. The lower vesical and lower urethral flaps sutured.
1. Edge of demobilized bladder. 2. Raw surface of demobilized bladder.

Millin and Read's (1950) technique has a better prospect of success and has the advantage over Aldridge's in that it does not open the vagina. Through a transverse abdominal incision the aponeurosis is exposed. Two strips each 1 cm. wide and 15–18 cm. long are cut from the aponeurosis of the external oblique, one on each side. The recti muscles are separated in the middle line and the retro-pubic space opened up. The bladder neck is identified and a tunnel is made behind the urethra. The strips are threaded through the outer borders of the recti on each side, then through the tunnel and then through the mid-rectus on each side, and sutured to each other by nylon sutures. Sling operations in general can only be adopted for the cure of incontinence following operations on fistulae of the trigone in the cases in which there is a reasonable chance of dissecting the neck of the bladder off the vaginal wall without subjecting the bladder and urethra to serious damage. It is of fundamental importance to choose the right case before attempting the operation.

We now come to the most troublesome type of all; the case in which the whole urethra has sloughed away. For the treatment of this condition Kelly suggested making a tunnel under the vestibule and drawing through it a long flap dissected from the anterior vaginal wall. Farrar improved this technique by dissecting a wider flap and converting it into a tube.

I have done these operations several times but I seldom effected a cure. A better procedure for the cure of such cases is Couvelaire's technique which was revived by Read. The operation is begun by making a preliminary cystotomy, then the fistula including the part of the urethra that may be present is completely mobilized and closed in 3 layers. A neo-urethra is constructed. After 3 weeks a special curved trocar is passed along it and the trigone is punctured. A catheter is directed through it into the bladder and left *in situ* until the cystotomy wound is closed.

Finally there remains a type of case in which hopeless destruction of vaginal tissues has occurred. In such cases implantation of the ureters into the sigmoid is advised. This operation, though easy to perform, has great disadvantages.

The operation is a serious procedure causing an anatomical change which imposes upon the bowel the additional function of a urinary reservoir.

As a result of this adjustment the upper urinary tract can be adversely affected. Ascending infection from the bowel occurs in most cases and usually leads to pyonephrosis. In a large number of cases biochemical disturbances occur owing to re-absorption of chlorides, urea and acids from the bowel. According to Ferris and Odel (1950) about 80 per cent of 141 patients who had both ureters transplanted developed acidosis with a high serum chloride and low bicarbonate concentration. Affected patients suffered from great thirst, and anorexia. There was a salty taste in the mouth, and the stools were large and watery. In many patients continual rectal drainage with a tube became necessary.

In order to evade the hazards and complications of transplanting the ureters into the colon C. Wells of Liverpool advised an alternative procedure in 1953. It consists of transplanting the ureters into an ileal loop isolated from the intestines and brought to the skin surface where the urine is collected in an ileostomy bag. This procedure was adopted by him with success in 9 cases of cystectomy for cancer of bladder.

Results

At the present day the cure of a mobile fistula of moderate size is an operation that can be successfully performed by gynaecological surgeons who have had experience in vaginal surgery. Immobile fistulae of the vault and fistulae tethered to the pelvic walls as well as urethral fistulae involving the neck of the bladder demand great experience in plastic vaginal surgery. In my early cases the failures were more common than the successes. I sometimes had to repeat the operation 3 or 4 times before I effected a cure. In my last 300 cases the results were invariably successful and almost always obtained at the first shot.

The figures illustrating the lecture are from the *Atlas of Mahfouz's Obstetric and Gynaecological Museum*, Volume Two, John Sherratt and Son, 1949.

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PHYSIOLOGICAL AND CLINICAL ASPECTS OF UTERINE ACTION*

BY

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NORMAL action of the uterus is desirable for preserving the health of a mother and her baby during labour. This function has been studied over the centuries and has given rise to much speculation, but it is particularly during the last decennium that it has become a subject of scientific investigation.

Abnormal uterine action in the absence of mechanical obstruction is one of the most pressing problems in the act of birth awaiting solution. The truth of the dictum of Leonardo da Vinci, expounded by him 500 years ago, ". . . . those who are enamoured of practice without science are like a pilot who goes into a ship without rudder or compass"—is well exemplified in the present scientific approach to this problem.

A. PHYSIOLOGICAL ASPECTS

It is obvious that the physiological intricacies of uterine action need first to be appreciated.

Innervation of the Human Uterus

Our knowledge of this subject is still far from complete. Many conclusions having been based on animal experiment it is difficult to know what to accept and what to discard. After a wide perusal of the literature Dr. J. Joseph, Reader in Anatomy at Guy's Hospital Medical School, has tried to bring order out of chaos and reached the following conclusions:

(1) There is an efferent nerve supply to the uterus and the parts of the uterus which can be influenced by these nerves are the muscle, blood vessels and the endometrium including glands.
(2) There is an afferent nerve supply from the uterus.
(3) Anatomical studies make it fairly clear that different parts of the uterus have separate nerve supplies (afferent and efferent)—fundus, corpus, cornua, lower uterine segment, cervix.
(4) It is very misleading to draw conclusions of the nervous system of the human uterus and its functions from animal experiments because in different states, for example, the pregnant and non-pregnant, the uterus of any one animal may react differently to the same stimulus or drug. There are considerable differences between the reactions of different animals (species difference) to the same experiment.

Caldeyro-Barciá and Alvarez (1954) have stimulated the pre-sacral nerve at the time of the operation of pre-sacral sympathectomy. They found in the non-pregnant state that, in general, the result of electrical stimulation was a bi-phasic response in the human uterus consisting of a contraction followed by a phase of inhibition. The changes were related to the stage in the menstrual cycle and it is interesting also to note that the responses of the corpus and of the cervix were very similar although sometimes the initial contraction of the cervix was smaller and at other times it was absent; the lowering of the cervical tone was greater than that of the corpus.

Further elucidation of the innervation of the human uterus has resulted from the use of caudal analgesia in labour. Johnson (1954) has

* Address to Edinburgh Obstetrical Society on 14th March, 1956.

made a special study of the treatment of disordered uterine function by this means and concludes that "both the motor and the sensory connexions to the pelvic floor and perineum arising from the sacral plexus are effectively blocked, together with the visceromotor parasympathetic connexions to the cervix. The upward extension of analgesia to the tenth dorsal segment in the extra-dural space interrupts the sensory connexions to the fundus uteri which enter the cord at this level, and the uterine action becomes painless. The sympathetic visceromotor fibres of the fundus uteri arising from the cord higher up, in the region of the fifth dorsal segment, are uninfluenced by caudal analgesia, while the opposing parasympathetic fibres from the sacral plexus below are paralysed."

The Biochemistry of the Myometrium

Csapo (1955) is of the opinion that functional myometrial disorders are responsible for spontaneous abortion, premature labour, uterine inertia and atony. He states that according to the conservative estimate of G. W. Anderson, of the Johns Hopkins Medical School (personal communication), in the U.S.A. in 1950 10 per cent of all pregnancies ended in spontaneous abortion and 7 per cent in premature labour. He estimated that 33 per cent of these abortions and 60 per cent of the premature deliveries are caused by functional myometrial disorders. This gave a total figure of over 250,000 representing an avoidable wastage of 54 per cent.

The total foetal, neonatal and maternal death rates resulting from functional myometrial disorders were estimated to comprise about 118,000 spontaneous abortions, about 48,000 deaths of premature babies, 21,000 foetal deaths resulting from abruptio placentae and inertia and 536 maternal deaths due to haemorrhage. The total figure was over 180,000. These figures serve to emphasize the important part the myometrium plays in pregnancy and birth.

Csapo has shown that myometrial function is regulated by ovarian steroids and that these influence the concentration of actomyosin, adenotriphosphate and ions. Oestrogen is essential for the synthesis of these substances and for ionic stability. He considers that "the oestrogen-dominated uterus at rest contains more potassium inside the cell than is optimal for the development of maximum tension. If the uterus is repeatedly stimulated some intracellular potassium is lost and consequently tension increases."

Plasma biochemistry in the study of uterine activity has so far been rather disappointing. We have, therefore, turned our attention to the uterine muscle itself. For the past year, Dr. D. F. Hawkins, working in our department, has been engaged in a study of the electrolytes in the *human* uterine muscle cell, with a view to establishing the electrolyte composition of the myometrial cell. At the time of Caesarean section or hysterotomy a small biopsy was taken from the edge of the incision.

The results to date are summarized in Tables I and II. These are only preliminary but are suggestive that such an approach may be

TABLE I
Potassium/Sodium Ratios in Early Pregnancy and At Term

	Uterine Muscle				
		Intracellular Levels m. eq./kg.			
	Cases	Na^+	K^+	Ratio K^+/Na^+	
Early Pregnancy:					
3–5 months	6	14	57	4·1	Oestrogen
At Term:					
Not in labour	13	20	53	2·6	Progesterone
In labour	3	14	40	2·9	
Long labour	5	17	36	2·1	

TABLE II
Potassium/Sodium Ratios With or Without Pre-eclampsia

	Uterine Muscle Estimated Intracellular K^+/Na^+ Ratios			
	Pre-eclampsia		No Pre-eclampsia	
	Cases	Ratio	Cases	Ratio
At Term:				
Not in labour	9	5·3	13	2·6
In labour	3	6·4	3	2·9
Long labour	2	3·7	5	2·1

interesting. It may be recalled that Horvath (1954) has shown in animal studies that the intracellular potassium-sodium ratio is 5 or 6 in the oestrogen-dominated uterus, while it is as low as 2 or 3 in the uterus dominated by progesterone. From Table I it would appear that in early pregnancy the uterus is dominated by oestrogen activity. At term there seems to be a loss of this marked oestrogen domination. Other studies suggest that hormonal changes occur shortly before term; in one or two cases the potassium/sodium ratio was still high at the 35th week. It is to be noted that there is no abrupt change in the ratio with the onset of labour and in the 5 cases of long labour the ratio was still low.

The data in Table II refer to cases at term with and without pre-eclampsia. The patients are classified, whether or not they were in labour; a further group who had long labours is included. In each of these groups the potassium/sodium ratio was markedly higher in the cases of pre-eclampsia. This suggests that the myometrial electrolyte balance in pre-eclampsia is markedly disturbed. Byron's description of *homo sapiens* was not so inaccurate.

". . . these sodas or magnesias,
which form the bitter draught, the human species."

(Don Juan, Canto LXXIII)

A different approach has recently been made by Tyler and Dicker (1956) working in the Department of Pharmacology at University College, London, who have investigated an "enzyme" in the blood serum or plasma of pregnant women capable of inactivating oxytocin *in vitro*. It seems that the prolongation of pregnancy to term is determined by the amount of this enzyme in the blood.

The work is in its preliminary stages but it is interesting that these workers have reported that at the end of pregnancy the inactivating substance disappears and that in those women who have a short first stage of labour there is no oxytocic-inactivating property in the last week of pregnancy. On the other hand, when labour was long, the plasma markedly inactivated oxytocin after the thirtieth week of pregnancy, or at term. After delivery, plasma levels returned to normal. This work is relevant to clinical practice in view of the increasing popularity and success of pitocin infusion for the treatment of uterine inertia. Perhaps the time is not far distant when a biochemical test may be evolved which will indicate whether the titre of "pitocinase" in the blood is normal or not. We would then know whether the pregnancy was near its end and whether uterine activity needed to be "boosted" by oxytocin therapy.

Histological Structure of Cervix Uteri and Pharmacological Response

Some of us agree with Bell and Nixon (1952) that the cervix is something more than the mere end of the uterus. Hughesdon's (1952) histological studies of the human cervix have revealed the presence of functioning muscle tissue which can be activated by drugs.

Newton (1934) was the first to note that the cervix reacted to drugs and to suggest that the reaction might be different from the rest of the uterus. Schild, Fitzpatrick and Nixon (1951) confirmed this (Fig. 1), and Fitzpatrick (Fig. 2) has shown further that in ruminants the

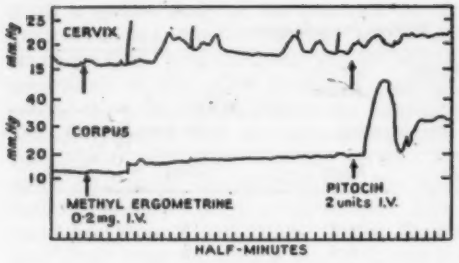

FIG. 1

Selective response of cervix uteri to methyl ergometrine. Effect of pitocin on corpus.

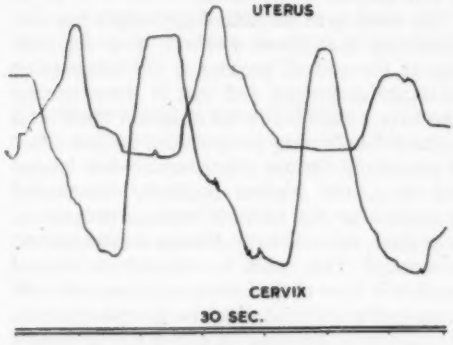

FIG. 2

Independence of cervical and corpus readings (cow). The cervix contraction is out of phase with the corpus. Such a pattern cannot be attributed to mechanical transmission of pressure from corpus to cervix.

response of the cervix is often dissimilar to that of the corpus with such drugs as oxytocin, vasopressin, ergometrine, adrenaline, and sympathomimetic amines. There is a greater response of the cervix than the corpus to ergometrine. This may be the reason for the placenta being trapped in the cervical canal when ergometrine in the human is given with the birth of the baby.

B. Hydrostatics of Uterus and Their Clinical Application

One of us (C.N.S.) has made extensive use of hydrostatic measurements over the past four years and has followed with interest, and often experimental repetition, the work of the leading physiologists on uterine action. The correct interpretation of Reynolds's (1949) fundal dominance, of Alvarez and Caldeyro's (1950) microballoon recordings, of Karlson (1949) and Ingelman-Sundberg and Lindgren's (1955) intrauterine gauges have presented us with considerable theoretical difficulties and left us with certain well-reasoned doubts about the conclusions which can rightly be drawn from such detailed studies of action in different parts of the uterine wall. There are, however, certain measurements of a gross character which can be made and which give an overall evaluation of the forces available for expulsion of the child and of the forces brought to bear to dilate the cervix. The first is the rise in amniotic pressure which can only be made on a uterus containing some free fluid (i.e., membranes intact or ineffectively ruptured). The second measurement is the pressure of the presenting part upon the dilating cervix. The Carey (1954) and Williams and Stallworthy (1952) technique of introducing a catheter *per vaginam* to measure the intra-amniotic pressure is accurate but inconvenient. When we tried this method a few years ago we found that existing external tocographs did not make an accurate assessment of intra-amniotic pressure. Their recordings were influenced by uterine forward rotation, and by changes in uterine wall thickness during contractions.

An instrument has now been designed which when applied to the abdominal wall measures the amniotic pressure within with accuracy equal to amniotic catheterization under all conditions. Figure 3 shows this instrument in use, and Figure 4 shows its principle of action. A perspex plate turns an area of abdominal wall into a flat surface. The instrument measures the force on a small area in the centre of this flattened part. Thus the measurement does not involve any bending of tissues, nor does muscle tension affect the accuracy. Figure 4 also records a direct comparison between internal (intra-amniotic) and external pressures. The difference in base line is because the one gauge is measuring pressure at the level of the umbilicus and the other at the level of the sacrum. This is a difference of 10 cm. water and is as significant as uterine tone in adding pressure to the cervix.

FIG. 3

Smyth "guard-ring tocograph" applied to abdominal wall (triplets).

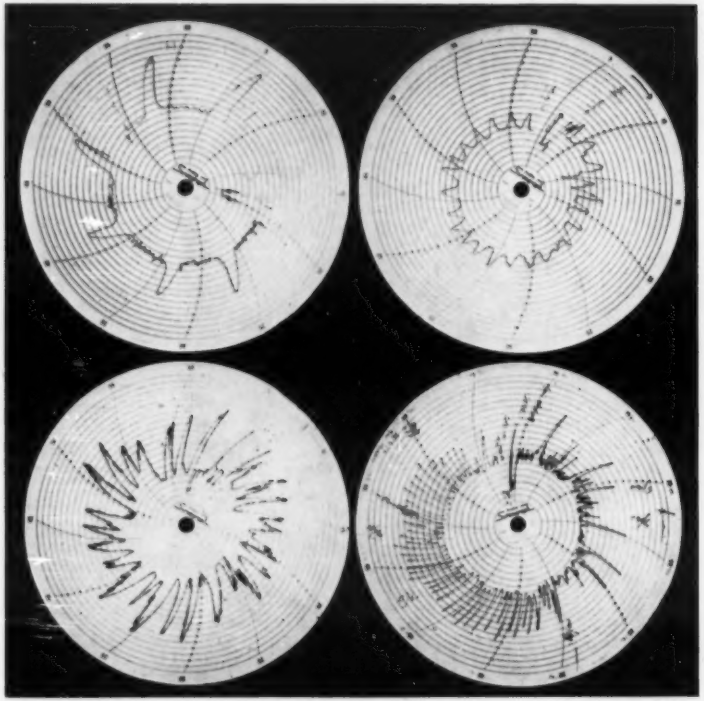

FIG. 6

Varying patterns of uterine contractility in long labour (48 hours). Lower right-hand graph shows effect of pitocin infusion.

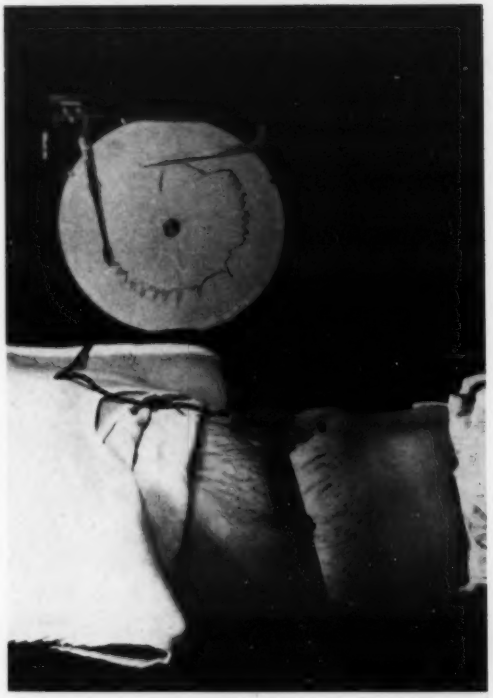

FIG. 7

External tocograph applied to post-partum uterus for quantitative assay of oxytocic drugs.

Oxyto
intrav

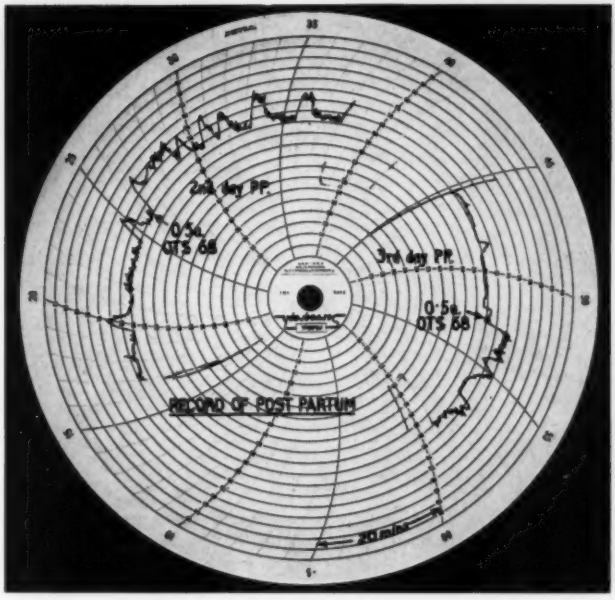

FIG. 8

Post-partum tocograph tracing showing effect of synthetic oxytocin (OTS 68—Sandoz). Effect equivalent to natural "pitocin" (Parke Davis).

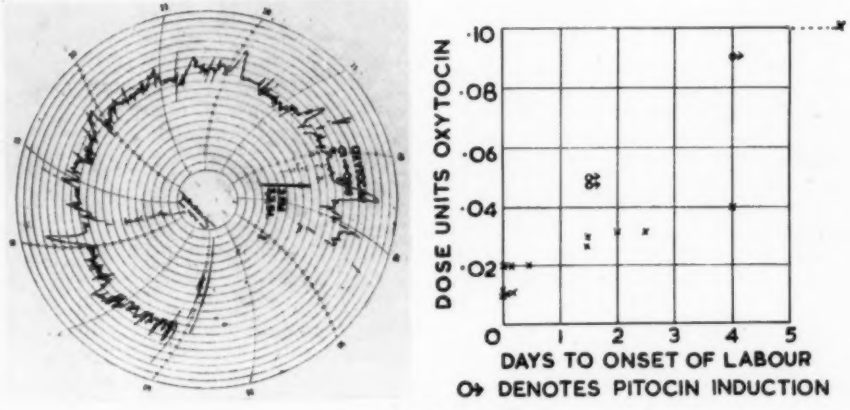

FIG. 9

Oxytocin (Pitocin) Sensitivity Test. The response of the uterus to small doses of oxytocin given intravenously at a standard rate (0·01 unit/minute) tends to increase as labour approaches. Arrow (O→) denotes pitocin induction.

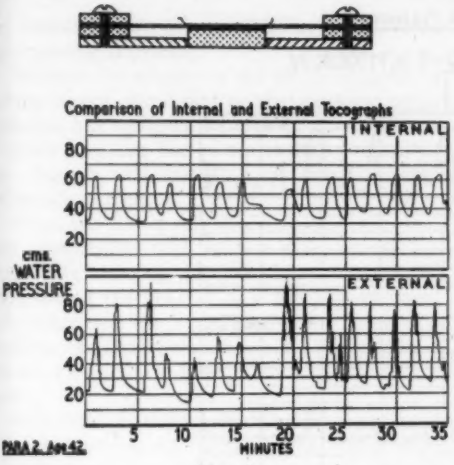

FIG. 4

Cross-section of guard-ring tocograph. Comparison of intra-amniotic pressure by internal and external measurement. Note similarity.

Uterine tone is of the same order of magnitude, i.e., 12 to 20 cm. water at umbilical level and indicates the value of the erect position in the first stage of labour. With this device we are able therefore with accuracy and certainty to follow the efficiency of uterine contractions throughout labour without any inconvenience to the mother or any risk of introducing infection into or traumatizing the uterus.

This new instrument can be used to diagnose uterine inertia, to control the infusion of oxytocin, and to investigate dystocia. The sharp peaks are transient intra-uterine pressure fluctuations not recorded by the slowly responding catheter gauge. They arise from foetal movements or changes in intra-abdominal pressure, e.g., bearing down or coughing.

Coupled with this measurement we measure whenever desirable the pressure of the presenting part upon the cervix. This work was first reported at the International Congress of Obstetrics in Geneva (Smyth, 1954). It has now been followed by a very much more comprehensive study by Lindgren (1955). There can be no doubt that in normal labour the fundal contractions cause the foetal head to bear on the cervix, and that firm contact between the cervix and presenting part, be it foetus or membranes with forewaters, is necessary for dilatation. Figure 5 shows a simultaneous record of fundal and head to cervix pressures during labour. The upper tracing is interesting since it was made during a normal, speedy and practically painless labour in a primigravida and shows activity in the cervix independent of fundal activity with initiation of all contractions at cervical level. With the administration of a test dose of oxytocin (0·01 unit/minute) all these cervical contractions spread to the fundus also. Figure 6 shows the varying contraction patterns encountered in long as in short labours and the effect of pitocin on the frequency of contractions. It illustrates how impossible it is to predict the duration of labour from the contraction pattern alone.

If the presenting part does not press rhythmically upon the cervix then the reason must be sought and where possible remedied. When there is no inertia recorded by the tocograph, then the fault may be with tough membranes, uterine "cuddling", high head, tight uterine attachments (ligaments).

Although measurements are desirable for accurate assessment we recommend a vaginal examination during at least one contraction with the finger placed between the head and cervix or forewaters, to feel the concurrent rise in head to cervix pressure. During this manœuvre motility of the head (slight ascent or descent) can be noted unless it is unusually tightly fixed in the pelvis.

If contractions are not present it is possible to induce one by gentle stimulation of the cervix digitally, by fundal palpation, or by the administration of an intravenous injection of oxytocin (0·01 unit/minute) to a maximum dose of 0·1 unit. The cervix will not dilate until pressure is brought to bear upon it from within. Adequate pressure cannot be produced unless the amniotic pressure rises to about 50 cm. water pressure (40 mm. Hg).

When the membranes are effectively ruptured there is no longer any intra-amniotic pressure but the uterine wall is festooned around the foetus. No practical study of the uterine wall now can tell whether the uterine action will be efficient, i.e., productive of a downward force

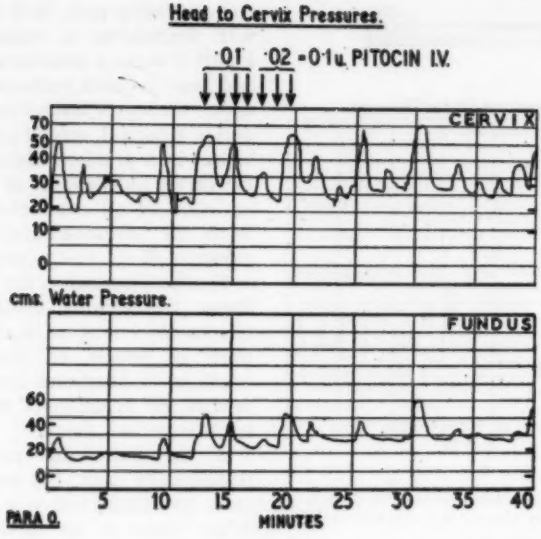

FIG. 5

Head to cervix pressure. Contractions of cervix independent of corpus activity.

upon the cervix. The head to cervix pressure is now the only criterion of efficient uterine action and should be measured.

With ruptured membranes, intra-amniotic pressure gauges and external tocograph alike only give a vague impression of uterine action; they remain useful for timing contractions but do not assess the strength of such contractions.

Head to cervix measurements show the resultant downward pressure upon the foetus but do not give any idea of the tightness with which the foetal trunk may be being compressed by the upper segment, i.e., active uterine retention or uterine "cuddling". Intra-uterine balloons will measure localized pressures but in general are not capable of rapid interpretation in relation to a given case.

A study of the hydrostatics of labour has led us:

(1) To the controlled use of oxytocic drugs to obtain adequate rise and fall of intra-amniotic pressure.
(2) To preserve the membranes intact to prevent uterine "cuddling" and to help in the early stages of dilating the cervix (artificial rupture of membranes contra-indicated when os is closed).
(3) To measure head-to-cervix pressure if reasonable contractions are not leading to progress and then to rupture membranes (low) if these seem to be holding the head back. If the head-to-cervix pressures still remain low, an intra-partum radiological examination of the pelvis is indicated to exclude cephalo-pelvic disproportion.

From the histology of the cervix we know also that the muscle cells have a fibrous sheath, the sarcolemma, and that they lie in a reticulum of connective tissue. This connective tissue contains fibres of collagen. These in themselves are practically inextensible but they are loosely attached to each other by polysaccharide "glues", and in the softened cervix there can be no doubt that the adhesiveness of the fibres of the collagen is loosened.

The cervix softens before it dilates or as it dilates. Is this softening hormonal in its origin or is it secondary to the rhythmical stretching

by Braxton Hicks contractions or both? These are pressing problems.

Whether the muscle in the cervix is active in labour or not, it can play no part until the cervix collagen has softened, since the forces required forcibly to dilate the os are vastly in excess of the strength available from the small amounts of muscle present.

When the cervix has softened, however, it is not improbable that muscle may attempt to delay the dilating process for at the small diameter of the internal os it has a mechanical advantage over the fundus, just as the nipple of a balloon lies flaccid even when the body is fully blown, although the pressure in both parts is the same.

Why does the cervix return to a shape somewhat resembling its former self a short while after delivery? Is it then that the sparse, smooth muscle cells exert their influence, as the upholders of structural form for the collagenous matrix? If this is so, how important is it that the muscle spindles should not be torn or overstretched in dilatation but merely loosened from each other for the time being?

We are at present working on this question of cervical dilatability and there is still much to learn. Hyalase, local anaesthetics, adrenaline, etc., have been injected into the cervix in labour with varying reports of success. Relaxin influences the cervix of mice—what of its effect on the human cervix, or is raspberry leaf-tea a more effective "cervical softener"!

Biological Assay of Oxytocic Drugs on the Human Uterus

Myerscough and Schild (1955) have used external tocography of the post-partum uterus for the quantitative assay of oxytocic drugs, with an apparatus (Fig. 7) designed by one of us (C.N.S.). They reported in 1955 their preliminary results at a symposium on "Dynamics of the Uterus and their Clinical Application", arranged by the Section of Obstetrics of the Royal Society of Medicine. They compared the activity of ergometrine and methyl-ergometrine and found the former to be more active. They also tested several new compounds claimed to possess oxytocic action. Since their publication we have recently been supplied by Sandoz Limited with samples of synthetic oxytocin (OTS 68). We have compared this preparation with natural "pitocin" (Parke Davis) in about 60 cases (post-partum) and within the limits of accuracy of our observations there is no significant difference in oxytocic effect and no side effects have been noticed in the doses given (up to 1 unit intravenously). There has been no alteration in the blood pressure using clinical methods of observation. The post-partum series shows that the two drugs are practically equivalent (Fig. 8).

C. Clinical Aspects

Pitocin Sensitivity Test, Induction of Labour and Condition of Cervix Uteri

One of us (C.N.S.) has designed a diagnostic test for the imminence of labour; it serves two useful purposes. Firstly, it differentiates those patients who will shortly start spontaneous labour and those who will not. The latter group can be divided clinically into those patients in whom no action is necessary (the "go-home" group), and those who should be induced for indications such as toxaemia, postmaturity, etc. Secondly, this test in labour induction indicates those cases which are insensitive to oxytocin, with the consequence that spontaneous contractions will be delayed. It is in this group that we prefer to re-inforce the surgical induction with an oxytocic infusion (our figure for the differentiation is 0·03 unit of oxytocin I.V.). Figure 9 shows the relationship of this test to the onset of spontaneous labour.

The rationale of the test is that with the imminence of labour the level of pitocinase (pitocin-inactivating substance) in the blood diminishes and that of active pitocin rises. The level may be supplemented by an infusion and will usually need to be at a rate of 1/200 to 1/50 unit per minute. This hormone initiates but does not increase the strength of uterine contractions —it just pulls the trigger by acting on the muscle cell membranes. Consequently it is of value when contractions are infrequent but is of little use when their occurrence is already more than one in two minutes. Sometimes when a patient has an occasional strong contraction among weak ones the hormone will cause all contractions to

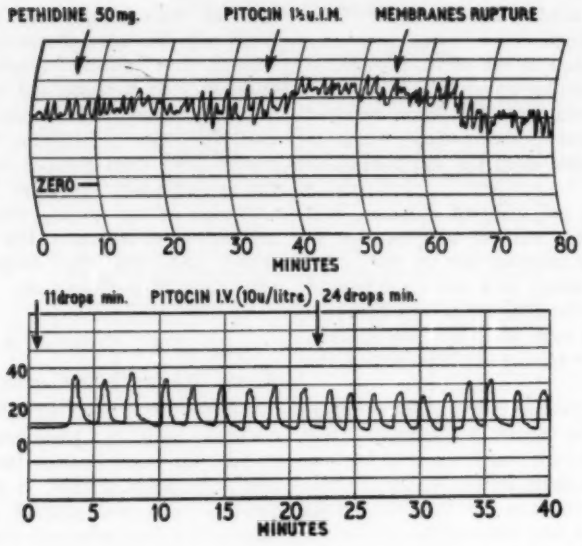

FIG. 10

Comparison of effect on uterine contractions of "pitocin" given by intramuscular or intravenous route.

assume full strength, i.e., generalized instead of localized uterine action. If too much is given at once the contractions ensue so rapidly that they run into one another and uterine tonus is raised to a dangerous level. It is for this reason that intravenous infusions with tocograph control are much safer than intramuscular injections of pitocin (Fig. 10).

Cocks (1955) has studied the condition of the cervix at the time of labour induction and related this to the subsequent course of labour. He investigated 133 cases at University College Obstetric Hospital and "typed" the cervix (Fig. 11). In Types 1 and 2 (ripe) the duration and complications of labour were statistically less than in the other types (unripe). The "sacral os" was responsible for a higher incidence of prolonged labour and surgical interference. Calkins (1954) has also stressed the importance of the firm cervix in association with prolonged labour.

In the light of these findings we have revised our procedure for induction of labour and our directions to medical staff are as follows:

Group A

If cervix soft, effaced (complete or incomplete), admits finger easily (Types 1 and 2—Cocks' classification)

then:

(1) Surgical induction either by membrane sweep and low rupture or membrane sweep only (high head) at 9 a.m.

(2) Pitocin sensitivity test.
If *sensitive* to 0·03 unit pitocin no further action for 24 hours and if not in labour then, pitocin infusion to be started.
If *insensitive* to 0·03 unit, pitocin infusion to be started.

Group B

If cervix NOT soft, NOT effaced, or "sacral os" difficult to insert finger (Type 3—Cocks' classification)

then:

Delay surgical induction. Commence pitocin infusion.

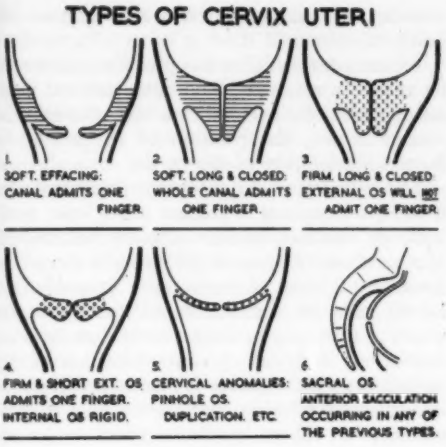
TYPES OF CERVIX UTERI
1.
SOFT. EFFACING: CANAL ADMITS ONE FINGER.
2.
SOFT. LONG & CLOSED: WHOLE CANAL ADMITS ONE FINGER.
3.
FIRM. LONG & CLOSED: EXTERNAL OS WILL NOT ADMIT ONE FINGER.
4.
FIRM & SHORT EXT. OS ADMITS ONE FINGER. INTERNAL OS RIGID.
5.
CERVICAL ANOMALIES: PINHOLE OS. DUPLICATION. ETC.
6.
SACRAL OS. ANTERIOR SACCULATION OCCURRING IN ANY OF THE PREVIOUS TYPES.

FIG. 11

Types of cervix in relation to subsequent course of labour.

Infusions should continue to 5 p.m. If at this time cervix is well dilated or delivery expected in a few hours, and if oxytocin is still necessary to maintain contractions, continue infusion; if, on the other hand, only slight progress, discontinue infusion and resume if necessary at 9 a.m. next day unless there is a contra-indication (foetal distress, high tone).

Vaginal examinations at noon and 5 p.m. in all patients.

Systematic Observations and Collation of Data Relating to Labour

We are beginning to appreciate the importance of accurate recording of data relating to labour. Since 1952 we have been using a punch card system. The information is collected partly from the patient's notes and partly from the patient herself, and requires considerable skill in winning the confidence of patients and in interpreting midwives' notes of labour progress.

To date, some 2,500 calculations have been made on the occurrence of 50 factors as functions of one another or as functions of the length of labour, of the patient's age, of parity, and so forth; many other inter-relationships could be explored. This work forms a guide not only to lines of treatment but to the probable profit of any investigation requiring a number of patients in a particular category. What has been perpetuated in textbooks and what has been accepted as facts by generations of obstetricians have now been found to be fallacious when exposed to the cold analysis of a punch card. This investigation has illustrated to us the great importance of averaging results over a large number of cases. Figure 12 shows the incidence

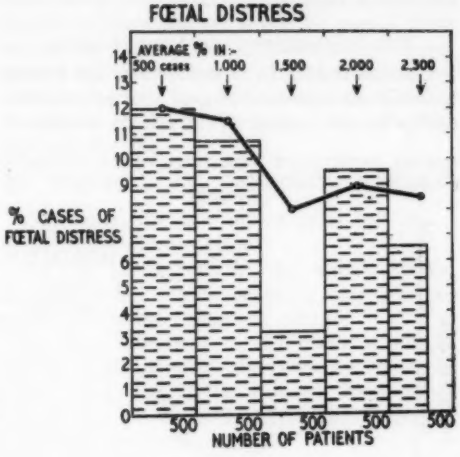

FIG. 12

Apparent variation in incidence of foetal distress when sample is too small.

of foetal distress, calculated for 500, 1,000, 1,500, 2,000, 2,400 deliveries and it is seen that the average result of 8·5 per cent might in a 500 case survey have been anywhere between 3 per cent and 12 per cent. The error of not having a large enough sample is obvious.

It has demonstrated that while the percentage incidence of many adverse factors increased with the length of labour, nevertheless the absolute incidence was vastly greater in normal and short labours and therefore these were the most profitable groups for study. For example, post-partum haemorrhage is only slightly increased in a long labour, whereas the very short labours, less than 5 hours, are the dangerous group. Another surprising finding was that within reasonable limits the weight (5–9 pounds) of the baby does not influence the length of

labour, neither does the intactness or not of the membranes. We have found also that the calculations for labour onset, as accepted in the U.S.A. —os 2 cm. in primiparae and 3 cm. in multiparae—on average gives a shorter labour than the criterion for labour onset of frequent painful contractions. In fact, an average 3 hours of labour contractions are required to take a primipara to 2 cm. dilatation and 2 hours to advance a multipara to 3 cm.

The Management of Long Labour

Labours lasting 36 or more hours are known to carry an increased risk of uterine infection and perinatal mortality (Fig. 13). In a series of

Fig. 13

Foetal mortality in relation to duration of labour (University College Obstetric Hospital).

20,000 deliveries at Queen Charlotte's Hospital labours exceeding 48 hours had an incidence of 3·1 per cent, and these were associated with a maternal mortality of 4·75 per 1,000 and a perinatal mortality of 120 per 1,000 (MacRae, 1949). More recently Sturrock and Brown (1956), in Edinburgh, have analyzed the results of prolonged first stage of labour (30 hours) and found that maternal morbidity, in spite of the use of antibiotics, was 5 times as high as the general rate for the hospital. Total foetal loss was 95 per 1,000. The old dictum that the duration of a labour should not be more than the interval between two sunsets—twenty-four hours—has much to commend it.

We consider that after this time the case should be carefully reviewed. An abdominal and vaginal examination will indicate the efficiency of uterine action, the position of the head, the degree of dilatation of the cervix.

The nutrition of the mother is important and if ketosis is present a glucose drip (5 per cent) with or without pitocin should be started. McCance and Colbourn (1955) have shown an increase in level of serum-urea in prolonged labour due to destruction of tissue protein which in turn may be the result of carbohydrate starvation. Our work on electrolytes is too early to indicate whether there is a serious imbalance of ions and whether electrolytes in a special combination should be administered.

We believe that if there is no advance in 24 hours despite good contractions an intrapartum radiological examination of the pelvis is indicated.

The use of oxytocin to stimulate uterine contractions is slowly being accepted in the treatment of uterine inertia. Theobald *et al.* (1948) were the first in Britain to use an intravenous infusion of oxytocin for this condition, but in a concentration that approximated to the physiological titre as found in the blood at the time of parturition. The intravenous route is safer than the intramuscular since the amount can be controlled by the rate of the drip. Llewellyn-Jones (1949), in Kuala Lumpur, has had success with this method in cases of uterine inertia (hypotonic). Moore and D'Esopo (1955), at the Sloane Hospital for Women, New York, have treated 215 cases of inertia, with a failure rate of 10 per cent.

We are convinced of the value of oxytocin drip infusion if there is lack of reasonable progress in cervical dilatation and the delay seems to be due to infrequency of strong contractions or if the case is one of "false labour", in which a normal labour pattern of contractions has been established and later has ceased.

Oxytocin Infusion

The infusion should consist of 5 units of oxytocin in 1 litre of 5 per cent dextrose.

The drip should commence at not more than

10 drops/minute with tocograph or phonocardiograph control or both. The rate should be increased gradually over the first half-hour until contractions occur, one every 2½ to 5 minutes or until there is a rise in the resting tone of the uterus, whichever is the less. The rate depends upon the condition of the veins as well as upon clamp tightness of the tubing. Sometimes the rate increases unexpectedly with danger to the foetus. For this reason patients having an infusion should not be left alone.

A ¼-hourly chart should be used to record drip rate, contractions rate and duration, blood pressure and foetal heart rate.

If at any time it is felt that the infusion has become unnecessary owing to contractions being firmly established, the rate should be slowed to 5 drops/minute so that the needle remains patent and if contractions continue for half an hour, the drip can be taken down. If a sustained uterine spasm develops then we suggest a subcutaneous injection (½–1 ml.) of adrenaline (1/1,000) rather than amyl nitrite which may cause a dangerous drop in blood pressure and consequent reduction of uteroplacental blood flow.

Duration of infusion also depends on the state of the cervix. Ideally the infusion should not be used unless the activity of the uterus can be recorded by a tocograph and this is usually not possible in domiciliary practice. There is no doubt that this treatment will diminish the incidence of Caesarean sections and forceps deliveries in cases of uterine inertia.

Caudal Analgesia

We have not had much experience of caudal analgesia but in the light of Johnson's (1954) favourable results with this treatment of disordered uterine function there seems to be a place for this therapy. It is a specialized technique and there should always be someone available in an obstetric clinic who is competent to practise it.

Caesarean section

Eventually a decision will have to be made as to whether this should be done. In the past obstetricians have delayed perhaps too long before adopting this method of terminating labour; it is a method which is no more than a mechanistic escape from a difficult situation. But this operation has saved lives and it will continue to rescue mothers and their babies from trauma, both physical and psychological. It is possible that an unnecessary Caesarean section may be done from time to time on a mother who given time might have been delivered vaginally with the aid of forceps. But that mother would never forget the ordeal of this vaginal delivery and she would be one of those who as the result of her travail would say "never again". We know that a fairly high number of women who have had difficult labours take contraceptive measures for the rest of their reproductive life.

Conclusion

Our experience over recent years has led us to the following conclusions:

(1) The lower pole of the uterus (cervix, isthmus, lower uterine segment) may play an *active* part in the process of labour.

(2) After labouring for 24 hours a mother should be placed under the care of a "dystocia team"; she should be isolated from other women in labour and radiological cephalopelvimetry arranged.

(3) The value of oxytocin drip infusion, with tocograph control, has been confirmed in the treatment of uterine inertia due to weak and infrequent contractions.

(4) Head-to-cervix pressure measurements are desirable when uterine contractions are adequate but dilatation is slow.

(5) There should be earlier resort to Caesarean section if oxytocin drip infusion and other medical treatment fails.

(6) It will be by the combined efforts of a team consisting of an obstetrician, pharmacologist, biochemist and a biophysicist, that progress will be made towards the solution of one of Nature's major mysteries—the process of birth.

Certain aspects of this work have been made possible through the generosity of the Nuffield Foundation. The tocodynamometer described has been the subject of a British Patent application by the National Research and Development Corporation.

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TUBO-UTERINE IMPLANTATION

BY

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IN all polyclinics endowed with a department devoted to the study of infertility there will frequently be seen two types of patient.

In the one, the patient as a rule is overweight, the uterus is fixed and there is easily palpable tubo-uterine pathology. Possibly there may exist a suspicion of tuberculosis.

In this type whatever operation is performed for infertility, whether it be the cuff one, the spoon salpingostomy, fimbriolysis, or perhaps the more extensive techniques of Topkins, Frenkel and Siegler (1956) or that of Cross and Erskine (1956), the prognosis is very disappointing. Indeed, all such operations have proved so discouraging that some surgeons, influenced by the pessimistic statistics of Greenhill (1937), Te Linde (1946) and Siegler and Hellman (1956), have given up all attempts to preserve tubal integrity and function. There is perhaps one exception to this negative attitude, namely the so-called phimotic tube with incurved fimbriae, the opening up of which, with or without the use of cortisone or glycerine locally, has given not less than a 12 per cent conceptional success.

In the other type, however, the patient is slim, young, intelligent and often beautiful. There is usually a story of abortion, criminal or induced, before or in the early years of matrimony, with or without cover by antibiotics. Sometimes she may give a history of classical Caesarean section, placenta praevia or only simple curettage. Occasionally there is a story of ligation of the tubes.

In this type, on examination nothing pathological whatever can be palpated, and, when investigated radiographically, cornual occlusion is seen to exist. When Rubin's CO_2 gas test is done, any pain entailed is entirely central and suprapubic. In these as repeated tests confirm the above findings any question of spasmodic occlusion can be ruled out.

The prognosis and treatment of this type is quite another matter, for, when the above history and clinical findings are confirmed at laparotomy, it will be seen that there is a fibrous nodular block at the cornu, or for the first inch only of the isthmus, probably the result of streptococcal infection of the endometrium or secundines. Most important of all it will be observed that the distal two-thirds of the tubes are perfectly healthy without thickening, kinking or adhesions, the fimbriae and ovaries being equally normal to the naked eye (Fig. 9).

These are ideal cases for tubo-uterine implantation which will give a 35–40 per cent pregnancy success rate, provided the surgeon has the experience, the special instruments and solid polythene (P.T.F.E.) 1·2 mm. in thickness.

Figures 1, 2 and 3 are sufficient to demonstrate the type; whereas Figures 4, 5 and 6 show the scheme of the operation. Figure 7 represents a posterior view of the implanted tube *in utero* with the polythene *in situ* down to the cervix. Figure 8 depicts the instruments used.

Extended experience has made clear that there are a few points of importance, which, if observed, will make for greater success:

(1) Operate immediately after cessation of a period.

(2) Two days before and after operation antibiotics should be given.

(3) A Bonney Myomectomy Clamp to elevate and fix the uterus is of great help when reaming the cornua or securing the implanted tubes in the uterus with 000 catgut on atraumatic needles.

(4) Never use a knife or bistoury at the cornua for that incurs haemorrhage and subsequent heavy scarring from the ragged edges. This is avoided by making a smooth tunnel with a reamer.

(5) Modern surgery of the common bile duct

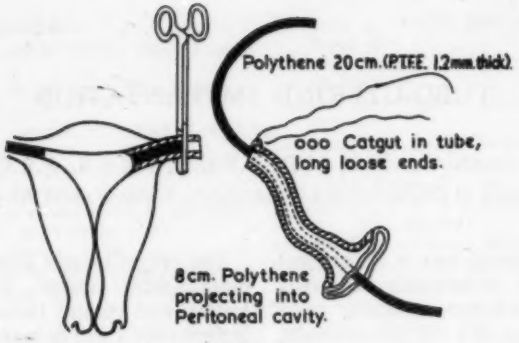

FIG. 4

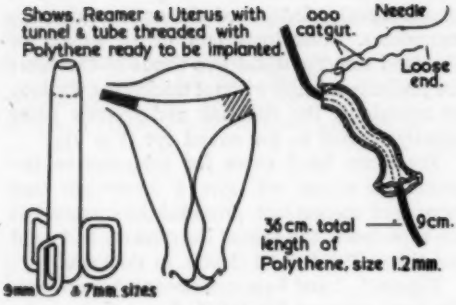
Shows. Reamer & Uterus with tunnel & tube threaded with Polythene ready to be implanted.
ooo catgut.
Needle
Loose end.
36cm. total length of Polythene, size 1.2mm.
9cm.
9mm & 7mm sites

FIG. 5

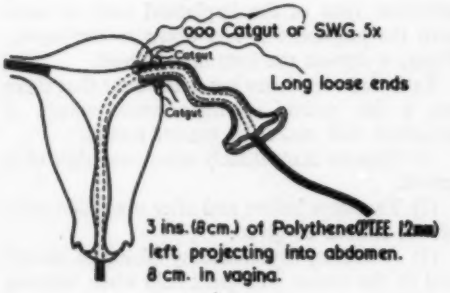
ooo Catgut or S.W.G. 5x
Catgut
Long loose ends
Catgut
3 ins. (8cm.) of Polythene(P.T.F.E. 1.2mm) left projecting into abdomen.
8 cm. in vagina.

FIG. 6

indicates that the polythene rods should be retained for 15–20 weeks and not so short a time as the 7 weeks originally advised.

(6) Sometimes it is not easy to pass the rods of polythene down through the uterus into the vagina. If that proves so, pass an 8-inch length of No. 4 polythene tubing through the reamer hole down into the vagina. The polythene rods can then readily be threaded down the tubing which an assistant draws into the vagina with 2 fingers.

(7) At the end of the operation, after inserting a speculum, the polythene rods are cut about an inch from the cervix.

(8) Always secure the ends of the P.T.F.E. to the infundibulo-pelvic ligaments.

To ventrosuspend the uterus before closing is advisable. The foot of the bed should be raised for 48 hours.

(9) Should polythene tubing be used because P.T.F.E. rods are not available, then it is essential that their ends should be closed by flaming before or during use. If this is not done there is the grave danger of capillary attraction of vaginal fluor and organisms into the peritoneal cavity setting up pelvic peritonitis.

(10) Shirokdar of Bombay, using the technique of Johnston (1955) of Melbourne, passes the P.T.F.E. rods from one threaded tube to the other across the endometrial fundus. This is easily done, but, despite removal rings and loops, the rod is not easy to extract 15–20 weeks later via the cervix.

I therefore prefer my own technique which entails no difficulty or pain at the time of removal.

(11) Out of 38 patients with the requisite history and findings who have been operated upon, 14 have gone to full-term, i.e., 36·1 per cent; 2 have aborted, giving a pregnancy rate of

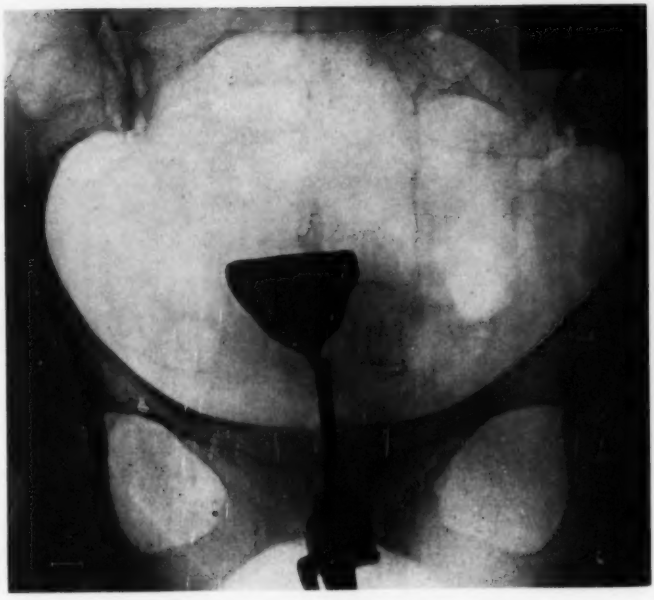

FIG. 1

Cornual occlusion subsequent to criminal abortion before marriage.

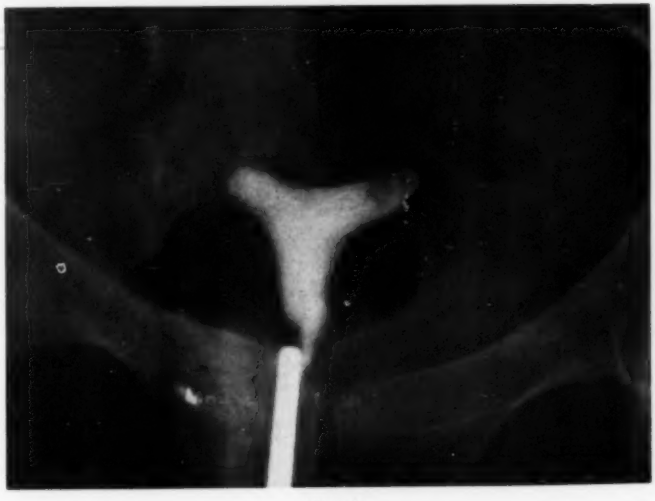

FIG. 2

Rounded cornua. Occlusion subsequent to induced abortion (incomplete) and later curettage.

FIG. 3

Isthmial occlusion after criminal abortion. Confirmed at operation. Distal two-thirds of tube absolutely normal.

FIG. 7

Bilateral tubo-uterine implantation in the cadaver with subsequent hysterectomy to show polythene *in situ*. Posterior view.

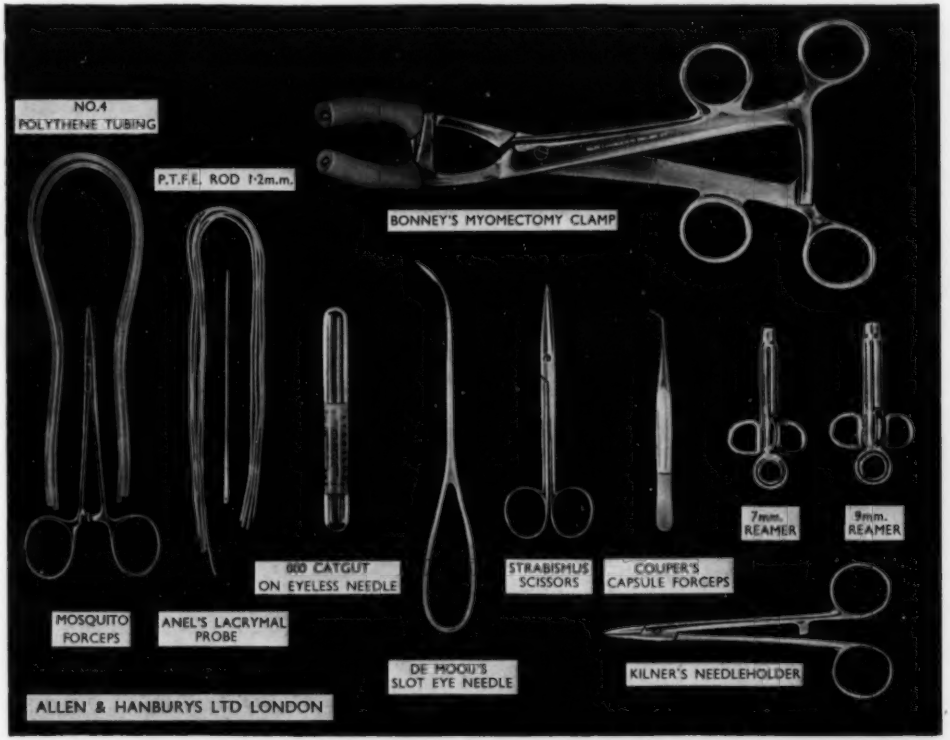

FIG. 8
Instruments required for operation.

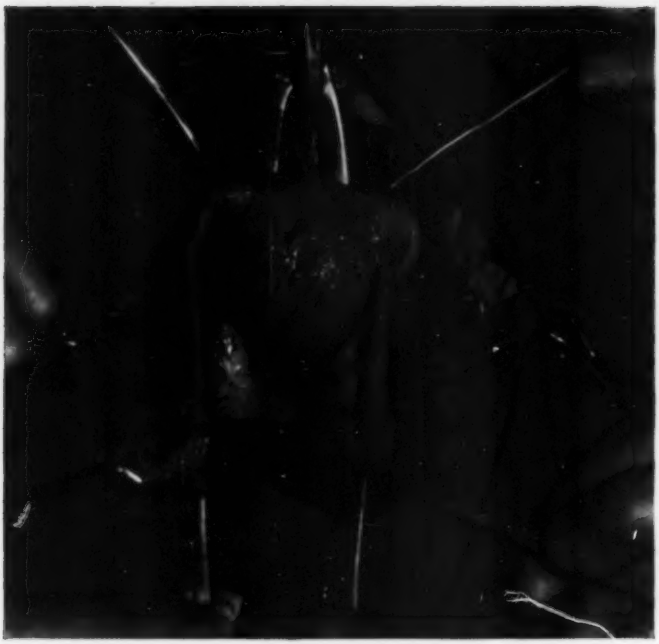

FIG. 9

Mrs. B., aged 24. Pre-marital evacuation of uterus at fourth month followed by fever and discharge for two weeks. Note fibrous nodules at cornua. Ovaries and distal two-thirds of tubes perfectly healthy. Probes show blockage 4 cm. from cornua.

FIG. 10

Mrs. J., aged 27. Two abortions procured. Note cornual and isthmial occlusions on proximal side of forceps, with probes showing normal distal portions of both tubes. Ovaries perfectly healthy.

42·2 per cent, which it is hoped will rise to 50 per cent in due course. There was one ectopic pregnancy.

(12) Caesarean section if not otherwise indicated is perhaps the best means of delivery, for unless the membranes rupture prematurely there does exist a small chance of herniation or rupture at the site of the reamer tunnel with spill of liquor amnii into the peritoneal cavity.

I with to thank the Staff of the Hammersmith, the Lewisham and the Florence Nightingale Hospitals for their care and follow-up of these cases.

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ASSOCIATION BETWEEN CLIMACTERIC HAEMORRHAGE, CARCINOMA OF THE BODY OF THE UTERUS AND DIABETES MELLITUS

BY

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EVIDENCE has been adduced to show that excessive bleeding during the climacteric and a late menopause may be prodromal symptoms of carcinoma of the body of the uterus (Randall, 1945; Corscaden and Gusberg, 1947). Suggestions have been made that overactivity of the anterior pituitary may lead to different manifestations including fibroids, diabetes mellitus and carcinoma of the body of the uterus (Way, 1954). The writer argues that if both diabetes mellitus and carcinoma of the body of the uterus have a common aetiology in the overactivity of the anterior pituitary, they may be expected to have some features in common. The incidence of climacteric haemorrhage and the age of onset of the menopause have therefore been determined for a series of diabetics. Comparisons of these factors in diabetics and in patients suffering from carcinoma of the body of the uterus have been made with normal controls.

In addition, the incidence of diabetes mellitus among patients suffering from carcinoma of the body of the uterus, and the incidence of carcinoma of the body of the uterus among patients suffering from diabetes mellitus, have been examined.

METHOD

All the patients covered by these investigations were seen by the same investigator, so that whatever subjective element was present was uniform throughout. The investigations extended over a period of some nine months and were carried out at the Royal Salop Infirmary, Shrewsbury. The area served by the Infirmary is extensive and includes the whole of Shropshire and parts of Montgomeryshire and Radnorshire. The population of this area is about 260,000.

Three series of cases were investigated. One series consisted of patients in whom carcinoma of the body of the uterus had been diagnosed. Another series consisted of patients suffering from diabetes mellitus, while the third series was a random selection of normal women and was used as a control. In all, over 400 women were seen.

There were 55 cases in the carcinoma of the body of the uterus series, and each one of them had had the diagnosis confirmed histologically. They were, in fact, mostly patients who were periodically attending the carcinoma follow-up clinic. They were given appointments to attend the Out-patient Department in the early afternoon, and they were asked to refrain from eating or drinking anything after breakfast on the day they attended. Each patient was seen and a menstrual history taken, after which a modified glucose tolerance test was carried out. This was used merely as a screening test and, if the results were in any way abnormal, a full glucose tolerance test was performed, usually at a later date.

The patients in the diabetes series were proved diabetics attending the Diabetic Out-patient Clinic. They were seen by the investigator during one of their routine visits to this clinic. All adult females were interviewed and care was taken to avoid duplication. In this series there were 249 patients.

For the normal control series, female patients attending the fracture clinic and the Casualty

Department, and patients in the female general surgical ward and the female chronic wards were used. No selection was exercised and all adult female patients present when the investigator made one of his visits were included. Again, care was taken to avoid duplication.

Definitions

The age of the onset of the menopause is the age at which the patient's menstrual periods stop. The menstrual periods are said to have stopped when one year has elapsed since the last period.

In some women the periods stop abruptly without any previous alteration in the duration of flow, amount of flow or frequency of periods. In others, the duration and amount remain constant, but the frequency lessens; there are increasingly long intervals between periods until finally the periods cease altogether. In others the frequency stays constant, but at each period the amount and duration become less. In others the menstrual pattern at the climacteric takes on a combination of the second and third methods, that is to say, the periods progressively become more scanty and of shorter duration, while the intermenstrual intervals become longer.

It is those patients whose menstrual pattern at the climacteric takes the form of increasingly long intermenstrual intervals that cause difficulty in the determination of the age of the onset of the menopause. However, if one year is taken as the limit of the intermenstrual period at the climacteric, resumption of vaginal bleeding after this interval must be regarded as post-menopausal bleeding, and the previous vaginal

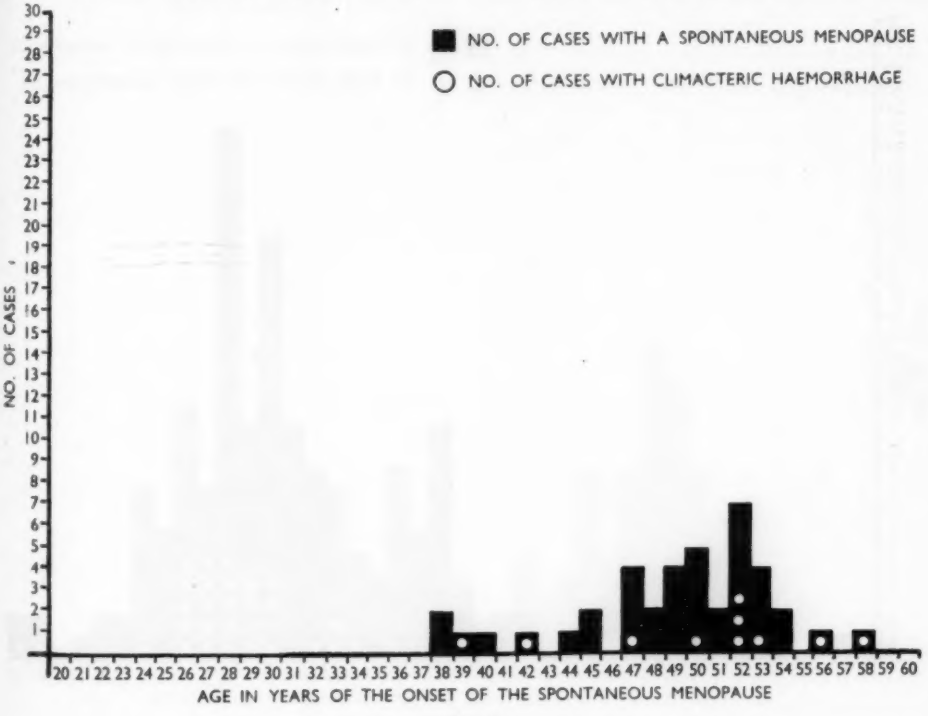

FIG. 1

Carcinoma of the body of the uterus series. The peak age of the onset of the menopause is at 52 years. There is a high incidence of climacteric haemorrhage among those patients with a late menopause.

bleeding must be regarded as the last true period.

Authors have used different terms to describe the condition called climacteric haemorrhage in this paper and in no case has a satisfactory definition of the condition been given. Randall (1945) called it pre-climacteric bleeding, menorrhagia at the climacteric and menorrhagia before the menopause. Corscaden and Gusberg (1947) called it excessive and irregular bleeding during the menopause.

The term climacteric haemorrhage has been adopted in this communication and it has been used to describe a change in the menstrual pattern occurring in women over 40 years of age, in whom the periods, more or less abruptly, become prolonged, heavy, more frequent and irregular, usually with clots. In some cases the periods end suddenly, coinciding with the termination of the climacteric haemorrhage. But this is not the usual history. In most cases the climacteric haemorrhage stops and more or less normal periods recur. Over a year or so these periods gradually tail off, until finally they cease entirely.

It happens that some women at the climacteric, whose periods are tailing off, have a heavy period lasting a day or two, after which the periods cease. This has not been considered to be climacteric haemorrhage.

In all cases, if the patient could not remember any part of the history, or if she appeared doubtful about it, this part of the history was omitted.

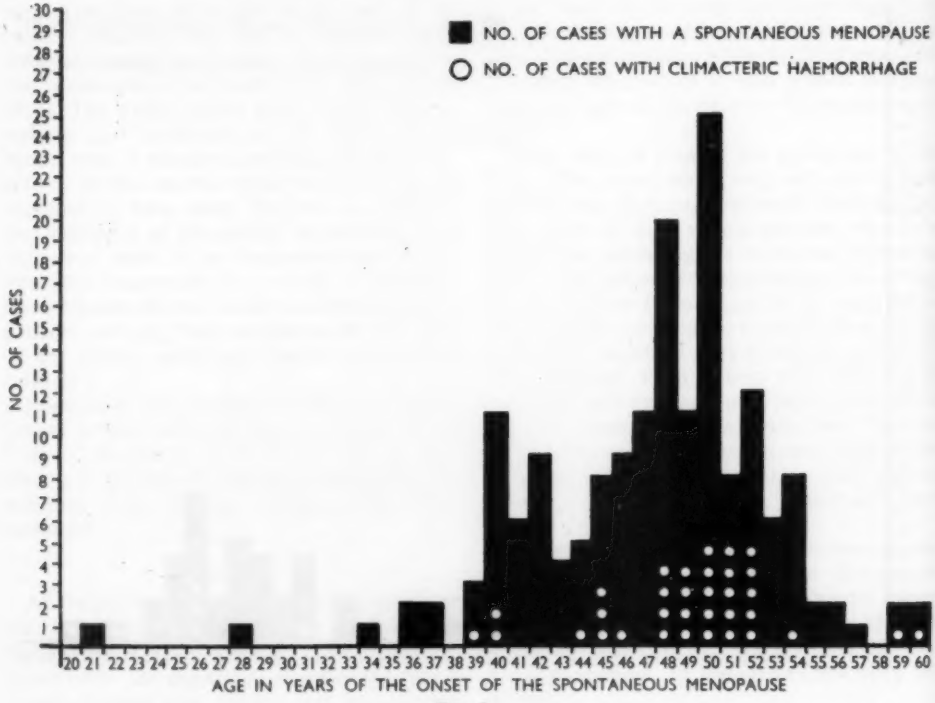
NO. OF CASES WITH A SPONTANEOUS MENOPAUSE
NO. OF CASES WITH CLIMACTERIC HAEMORRHAGE
NO. OF CASES
AGE IN YEARS OF THE ONSET OF THE SPONTANEOUS MENOPAUSE

FIG. 2

Diabetes series. The peak age of the onset of the menopause is at 50 years with a smaller peak at 40 years. There is a high incidence of climacteric haemorrhage among those patients with a late menopause.

Results

(a) *Age of the Menopause*

There were 55 cases of carcinoma of the body of the uterus in this series, and of these 40 had had a spontaneous menopause. Figure 1 shows the age incidence of the onset of the spontaneous menopause. The peak incidence is at the age of 52 years, and 22 out of the 40, or 55 per cent continued to menstruate after the age of 50 years.

Of the 249 diabetics seen, 172 had had a spontaneous menopause. Figure 2 shows a graph in which the number of menopauses occurring at each age is plotted against the ages at which the menopauses occurred. Sixty-eight of these patients, or 40 per cent, continued to menstruate after the age of 50 years. The peak age for the onset of the spontaneous menopause is 50 years, but there is a smaller peak at 40 years.

Of all the normal women that were used as controls, only 107 could give a reliable history regarding the age of the onset of the menopause and climacteric haemorrhage. The graph in Figure 3 demonstrates the age incidence of the onset of the spontaneous menopause. The peak age is 48 years, and only 29 out of the 107, or 27 per cent, continued to menstruate after the age of 50 years.

Thus, in patients suffering from diabetes mellitus and from carcinoma of the body of the uterus, the onset of the spontaneous menopause is later than in normal women.

(b) *Climacteric Haemorrhage*

The most common symptom of early car-

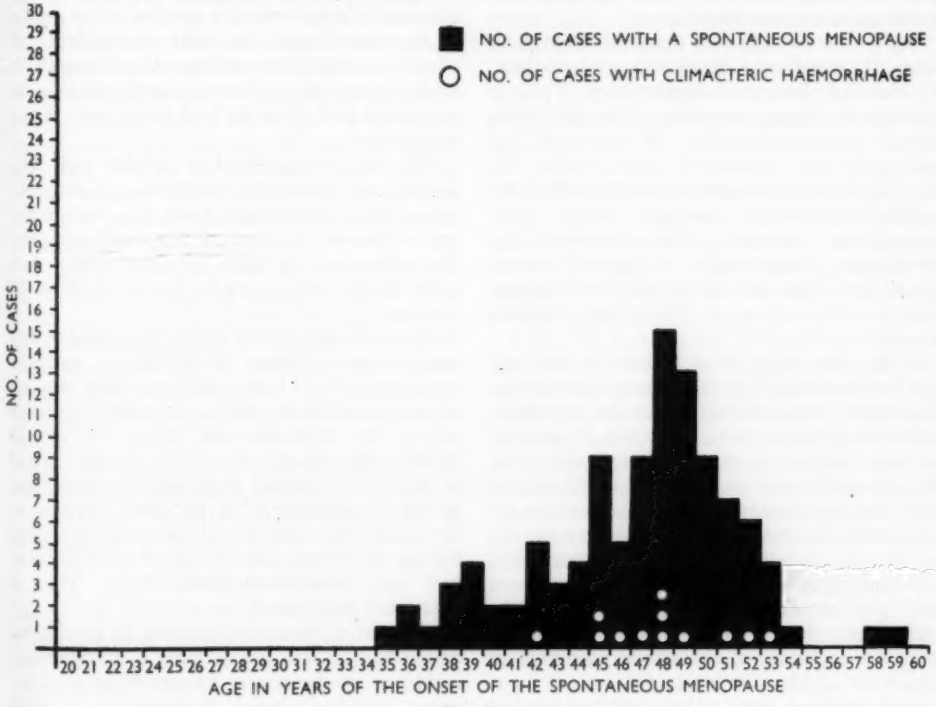
NO. OF CASES WITH A SPONTANEOUS MENOPAUSE
NO. OF CASES WITH CLIMACTERIC HAEMORRHAGE
NO. OF CASES
AGE IN YEARS OF THE ONSET OF THE SPONTANEOUS MENOPAUSE

FIG. 3

Normal control series. The peak age of the onset of the menopause is at 48 years. The incidence of climacteric haemorrhage is uniformly distributed.

cinoma of the body of the uterus is abnormal uterine bleeding. In those cases in which the carcinoma develops before the menopause, this abnormal uterine bleeding takes the form of intermenstrual haemorrhage. On the other hand, in those cases in which the carcinoma develops after the menopause, there may or there may not be a history of climacteric haemorrhage.

In the present series, there were 55 cases of carcinoma of the body of the uterus. Of these, 40 had had a spontaneous menopause, 3 had had radiation induced menopauses, one had had a bilateral oöphorectomy and 11 were still menstruating when the carcinoma developed.

Of the 11 patients who were still menstruating when the carcinoma developed, 10 had complained of irregular and excessive uterine haemorrhage, while 1 patient was symptom-free and the diagnosis was made by a routine curettage at a repair operation.

Forty-four patients had ceased to menstruate when the carcinoma developed, and of these, 13 had had climacteric haemorrhage. Thus, in patients developing carcinoma of the body of the uterus post-menopausally, 29 per cent had previously had climacteric haemorrhage. But the incidence of climacteric haemorrhage is not evenly distributed through these post-menopausal patients. The incidence of climacteric haemorrhage is greater among those with a late menopause than among those with an early menopause. This is well shown in Figure 1.

It has been shown that 52 years is the peak age for the onset of the spontaneous menopause in patients who subsequently develop carcinoma of the body of the uterus, and that 55 per cent of these patients continue to menstruate after the age of 50 years. In this series of 40 patients who had spontaneously ceased to menstruate, there were 18 who had done so before the age of 50 years, and of these 18 only 3 patients had had climacteric haemorrhage, giving an incidence of 17 per cent. For those with a late onset of the menopause, that is, at the age of 50 years or over, the incidence of climacteric haemorrhage was 7 out of 22 or 32 per cent.

In the diabetes series, 185 patients had reached the menopause, including the spontaneous and the artificial, and 46 out of these had had climacteric haemorrhage. The incidence of climacteric haemorrhage among diabetics is thus 25 per cent.

In order to relate the incidence of climacteric haemorrhage to the age of the onset of the menopause, only those patients who had had a spontaneous menopause were considered. In the whole diabetes series, there were 172 patients who had had a spontaneous menopause and, of these, 34 had had climacteric haemorrhage. It has been shown that there are two peak ages for the onset of the spontaneous menopause in diabetics, one at 40 years and the other at 50 years. If the graph showing the relation between climacteric haemorrhage and the age of the onset of the spontaneous menopause is superimposed on the graph showing the age incidence of the onset of the spontaneous menopause, as in Figure 2, it will be seen that the incidence of climacteric haemorrhage is greatest in the region of the second peak, i.e., that the incidence of climacteric haemorrhage is greater among those diabetics who have a late onset of the menopause compared with those with an early onset of the menopause.

This may be expressed in another way. The incidence of climacteric haemorrhage in diabetics who cease to menstruate early, i.e., before the age of 50 years, is 16 out of 104, or 15 per cent. The corresponding figure for those with a late onset of the menopause is 18 out of 68 or 27 per cent.

In the normal control group, consisting of 107 women, the incidence of climacteric haemorrhage was only 11 per cent and there was no indication that there was any increased incidence among any particular age group. Of the 78 women who ceased to menstruate before the age of 50 years, 9 had had climacteric haemorrhage, giving an incidence of 11 per cent. There were 29 women who had ceased to menstruate after the age of 50 years and of these, 3 or 10 per cent had had climacteric haemorrhage. This is illustrated in Figure 3.

Thus, in diabetes mellitus and in carcinoma of the body of the uterus there is an increased incidence of climacteric haemorrhage as compared with the normal. Furthermore, in both these conditions, but not in the control series, the incidence of climacteric haemorrhage is

greater among those patients with a late menopause as compared with those with an early onset of the menopause.

(c) *Incidence of Diabetes in the Carcinoma of the Body of the Uterus Series*

Of the 55 patients who were seen by the investigator, 50 attended at the laboratory for the glucose tolerance test. Of these 50 patients, 4 were found to be diabetic. The incidence of diabetes in this series of patients with carcinoma of the body of the uterus is 8 per cent. Of these 4 patients found to be diabetic, 3 had continued to menstruate after the age of 50 years, and one had ceased to menstruate at the age of 49 years.

There were also 5 other patients who had abnormal glucose tolerance curves, but these curves were not considered to be diabetic.

(d) *Incidence of Carcinoma of the Body of the Uterus in the Diabetes Series*

There were 249 adult female diabetics seen in this series and 16 of these gave a history of having had a hysterectomy. Of these 16 hysterectomies, 5 were for carcinoma of the body of the uterus, 6 were carried out for fibroids, and in 5 cases the patient could not give the indication for the hysterectomy.

In this series of diabetics, therefore, 2 per cent of the patients had had carcinoma of the body of the uterus and 2 per cent had had fibroids. In addition, there were the 5 cases in which the indication could not be discovered, and which would presumably increase the incidence of fibroids and/or of carcinoma of the body of the uterus.

The 249 diabetics were of all ages and the occurrence of additional cases of carcinoma of the body of the uterus in the future may be assumed.

Discussion

Age of the Onset of the Menopause

In the present control series, it was found that only 27 per cent of normal women continued to menstruate after the age of 50 years. This is in fairly close agreement with the figure of 29 per cent produced by the Medical Women's Federation who investigated the matter in 1933. The peak age of the menopause in the present series was at 48 years.

In patients with carcinoma of the body of the uterus, the peak age of the menopause is at 52 years and 55 per cent continue to menstruate after the age of 50 years. Corscaden and Gusberg (1947) also found evidence for a late cessation of the menses in patients who develop carcinoma of the body of the uterus. Their peak incidence was in the region of 52 to 54. Randall (1945), in his series of patients, found a late onset of the menopause. The age of onset of the menopause is thus significantly later in patients who develop carcinoma of the body of the uterus than it is in normal women.

The author has shown that in diabetics the peak age of the onset of the menopause is at 50 years, and that 40 per cent of patients continue to menstruate after the age of 50 years. Way (1954) also produced evidence for a late onset of the menopause in diabetics.

This late onset of the menopause is one of several features which are common to diabetics and patients who develop carcinoma of the body of the uterus.

Climacteric Haemorrhage

The author has shown that the incidence of climacteric haemorrhage among the normal female population is 11 per cent. Randall (1945) found an incidence of 13·3 per cent in his general population.

Of all the patients who develop carcinoma of the body of the uterus post-menopausally, the author has shown that 29 per cent had had climacteric haemorrhage. Randall (1945) also produced evidence to show a higher incidence of climacteric haemorrhage among patients who subsequently develop carcinoma of the body of the uterus post-menopausally as compared with the general population. Corscaden and Gusberg (1947) found that the incidence of excessive and irregular bleeding during the menopause was greater in the carcinoma of the body of the uterus group than in the general female population. Thirty-two patients, or 39 per cent, of the 82 who contracted the cancer after the menopause had suffered from abnormal uterine haemorrhage during the climacteric.

However, as a further step, the author has

related the incidence of climacteric haemorrhage to the age of onset of the menopause and has found that, in cases of carcinoma of the body of the uterus those patients with a late onset of the menopause have a higher incidence of climacteric haemorrhage than those with an early onset.

It follows that when a patient presents herself with a late onset of the menopause she has a greater chance of developing carcinoma of the body of the uterus, and, should this late onset of the menopause be associated with climacteric haemorrhage, the chances are even greater. This should be borne in mind when deciding, in cases of climacteric haemorrhage, whether treatment should be by hysterectomy or by a radiation induced artificial menopause.

It is unlikely that carcinoma is present at the time that the climacteric haemorrhage is manifesting itself. In several cases in the present series, there were intervals of more than 10 years between the cessation of the climacteric haemorrhage and the commencement of the post-menopausal bleeding which was the first symptom of the carcinoma. During this interval the patient was symptom-free.

The author could trace no previous work on the incidence of climacteric haemorrhage in diabetes. The present investigations reveal that, of all post-menopausal diabetics, 25 per cent had had climacteric haemorrhage. The incidence of climacteric haemorrhage in diabetics is thus almost the same as in patients who develop carcinoma of the uterine body post-menopausally. But the similarity goes farther. When the age of onset of the menopause was taken into consideration, it was found that the incidence of climacteric haemorrhage was higher among patients with a late onset of the menopause as compared with those with an early onset of the menopause.

This is another of the several features which are common to diabetes and carcinoma of the body of the uterus.

Incidence of Diabetes Mellitus in the Carcinoma of the Body of the Uterus Series

The author's incidence of 8 per cent of diabetics in his carcinoma of the body of the uterus series is low compared with the findings of other workers. Moss (1947), in a study of 23 cases, found that 5 showed a relatively severe diabetes and 10 a mild diabetes. Palmer *et al.* (1949) showed that 28 cases out of 165 were diabetic, an incidence of 16·9 per cent. In the series of Scheffey, Thudium and Farell (1943), the incidence of diabetics in a series of carcinoma of the body of the uterus cases was 14 out of 127, or 11 per cent. Among the patients discussed by Way (1954), 29 per cent were diabetic and 48 per cent were pre-diabetic.

It is possible that the discrepancies in the above figures may lie in different interpretations of the glucose tolerance curve. In any case, it does appear that there is a high proportion of diabetics among patients with carcinoma of the uterine body.

Incidence of Carcinoma of the Body of the Uterus in the Diabetes Series

It was found that 2 per cent of all adult female diabetics had had carcinoma of the uterine body. The crude death rate of carcinoma of the body of the uterus in 1951 was 5·2 per 100,000 of the total female population in England and Wales. It is almost impossible to obtain accurate figures for the incidence of carcinoma of the body of the uterus in the general female population (the morbidity rate for the disease). But it would seem that the incidence of 2 per cent is unduly high and must be of significance.

Association between Carcinoma of the Body of the Uterus and Diabetes Mellitus

That there is an association between carcinoma of the uterine body and diabetes mellitus has been made clear by these investigations. In both conditions there is a late onset of the menopause and a high incidence of climacteric haemorrhage, the latter having a higher incidence among those patients with a late menopause. In carcinoma of the uterine body, diabetes mellitus is not uncommon; and in diabetes mellitus carcinoma of the body of the uterus has a relatively high incidence.

Radiologically Induced Menopause and Subsequent Carcinoma of the Body of the Uterus

It has been shown that of all patients developing carcinoma of the body of the uterus post-

menopausally, 29 per cent had had climacteric haemorrhage. It is a fairly common gynaecological procedure to create an artificial menopause by radiological means or by radium irradiation, and several authors have drawn attention to the fact that carcinoma of the body of the uterus has occurred in patients who had previously been subjected to a radiation menopause.

Taylor and Becker (1947) report that, out of 463 cases of carcinoma of the body of the uterus, 23 or 4·97 per cent, had had an artificially induced menopause. They did not, however, state the indications for the artificial menopause nor the methods used.

Smith and Bowden (1948) found that, of 805 patients with pathologically proved cancer, there were 8 (0·99 per cent) to whom radium had been administered at least 10 years previously for pathologically proved benign uterine lesions. An analysis of the indications for the artificial menopause in these 8 cases is as follows:

Case 1. Diabetic, persistent periods at 60 years.
Case 2. Menorrhagia at 43 years.
Case 3. Irregular vaginal bleeding at 36 years.
Case 4. Irregular menses at 48 years.
Case 5. Vaginal bleeding at 47 years.
Case 6. Frequent menses at 43 years.
Case 7. Uterine fibroids at 47 years.
Case 8. Menorrhagia at 45 years.

In 5 cases, Cases 2, 4, 5, 6, and 8, the patients had symptoms which the writer would probably have classed as climacteric haemorrhage. These patients form part of a group of which a number spontaneously develop carcinoma of the body of the uterus some years later. From the investigations described in the present communication it would appear that these patients, whether or not they had been irradiated, would probably have developed the carcinoma.

The present author has already suggested that, in cases in which there was climacteric haemorrhage followed by a menopause and a subsequent development of carcinoma of the body of the uterus, it was unlikely that the carcinoma was present at the same time as the climacteric haemorrhage. The work of Smith and Bowden (1948) supplies evidence which supports this contention, for endometrial biopsies taken during the climacteric haemorrhage did not reveal malignancy, yet these patients developed carcinoma of the body of the uterus some years later.

Case 1 can be explained by the finding in the present paper that carcinoma of the body of the uterus is more common in diabetics than in the general population. Case 7 can be explained by the association between fibroids and carcinoma of the body of the uterus. It is more difficult to explain away Case 3.

Hertig and Sommers (1949) have made a study of 32 cases of carcinoma of the body of the uterus in which endometrial biopsies had been taken from 1 to 23 years before invasive carcinoma was diagnosed. They found that radiation therapy had been used in 20 out of these 32 cases at an average interval of 7 years before the development of the carcinoma. From this they concluded that radiation therapy of the uterus for benign conditions is followed by a greater than expected incidence of endometrial carcinoma.

It is unfortunate that no account is given in their paper of the indications for which radiation therapy was used. If, as is commonly the case, radiation therapy was used to induce an artificial menopause in patients with climacteric haemorrhage and a late continuation of the menses, then it was used in a group of patients in which it would be expected that a greater number than usual would spontaneously develop carcinoma of the body of the uterus. This explains the figure of these authors to be higher than expected.

It is the writer's opinion that there is no proof that a radiation induced menopause predisposes to carcinoma of the body of the uterus, but that the predisposition to carcinoma is more especially present in every case in which a late menopause has been associated with climacteric haemorrhage.

Conclusions

In diabetics and in patients having carcinoma of the body of the uterus there is a distinct tendency for a late menopause associated with climacteric haemorrhage. In the writer's opinion, cases presenting themselves for treatment for climacteric haemorrhage and a late menopause

should be subjected to a hysterectomy instead of radiation therapy unless some special reason exists why the major procedure should not be performed.

A radiation induced menopause does not predispose to subsequent carcinoma of the body of the uterus, but the predisposition to carcinoma is already present when the radiation is applied.

There is an association between diabetes and carcinoma of the body of the uterus.

Acknowledgments

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THE GUARD-RING TOCODYNAMOMETER

Absolute Measurement of Intra-Amniotic Pressure by a New Instrument

BY

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INTRODUCTION

THE measurement of intra-amniotic pressure is of value in obstetric practice for the diagnosis and controlled treatment of dystocia.

The hydrostatic pressure in the amniotic sac can be measured in absolute units by catheters, balloons and pressure transducers introduced into the uterus and suitably positioned within or without the membranes (Moir, 1934; Karlson, 1944; Williams and Stallworthy, 1952; Ingelman-Sundberg, Lindgren and Ljungström, 1953; Carey, 1954; Smyth, 1954; Lindgren, 1955). Despite their scientific perfection all these methods cause some degree of inconvenience to the patient and demand special attendance of the obstetrician.

To overcome the inconvenience of intra-uterine apparatus abdominal "tocometers" have been extensively used. There are many types of tocometer, such as those of Frey (1933), Lorand (1947) and Reynolds, Harris and Kaiser (1954), to mention only a few, but for various reasons inherent in their design and mounting upon the patient they do not record true intra-amniotic pressure. They are influenced by skin tension and by forces required to flex the skin and consequently are affected by forward uterine rotation during labour contractions. They have uses for timing contractions and noting changes in uterine tone during treatment of a patient but their readings do not necessarily correspond in intensity or in time with the rise and fall of intra-amniotic pressure.

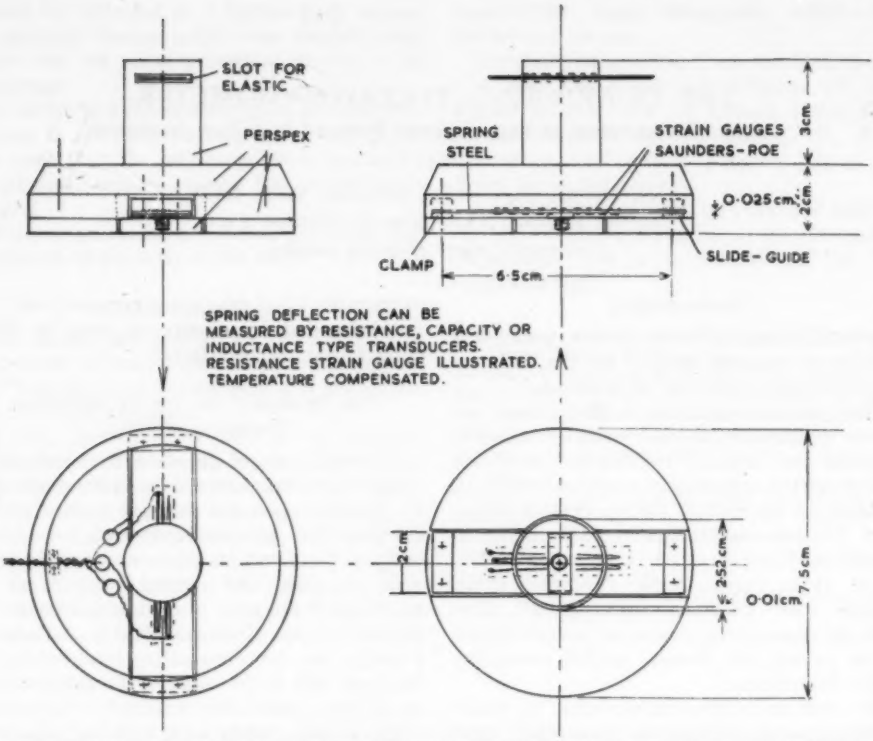
The new tocodynamometer overcomes the defects of earlier instruments and makes an absolute measurement of intra-amniotic pressure possible through the abdominal wall. Its accuracy is equal to that of intra-amniotic instruments ($\pm$ 1 cm. water pressure) and it is not influenced by obesity or even by being applied over the bed-clothes.

THE PRINCIPLE OF THE GUARD-RING TOCODYNAMOMETER

If a small area of the abdominal and underlying uterine wall is turned into a flat diaphragm by pressing upon the external surface with a flat plate the pressures upon each side of the body wall will be equal; by measuring the force upon the plate the internal pressure can be measured if the area of contact is known. To define the area of contact exactly and also to eliminate any pressures arising from bending of the body wall at the edges of the flattened area the pressure plate is surrounded by a guardplate which is held exactly level with the measuring area and flattens an additional "surround" of body tissues. The force on the "surround", or guard-ring, is not measured.

The instrument is drawn in Figure 1, and Figure 2 is a section of the instrument applied to the patient. The pressure-sensitive area, 5 sq. cm., in the centre and the guard-ring surrounding it are clearly shown.

The deflection of the spring, which is mounted upon the guard-ring and supports the central pressure-sensitive area, is taken as a reading of the force on the central area. The deflection is 0·025 cm. for an intra-amniotic pressure of 120 g./cm.^{2}, i.e., a very strong contraction. Ideally, there should be no deflection at all but the error introduced by so small a deflection is negligible when using the instrument on soft body tissues or over blankets. In the instrument shown the spring deflection is measured by resistance strain gauges adherent to the spring



TOCOGRAPH SMYTH GUARD-RING DESIGN FOR ABSOLUTE MEASUREMENT OF INTRA-UTERINE PRESSURE THROUGH ABDOMINAL WALL. 5 SQ. CM. PRESSURE SENSING AREA FLAT WITH RESPECT TO GUARD RING TO WITHIN 0·004 CM. DEFLECTION OF SPRING FOR 100 G. (20 G./CM.²) 0·004 CM. APRIL 1955

FIG. 1

Instrument Construction.

surfaces (see Fig. 1), but capacitance or inductance bridge methods would be equally suitable.

With the resistance strain gauge method the tocodynamometer is connected in a Wheatstone bridge circuit and joined to the input of a Honeywell-Brown potentiometric recorder of sensitivity 1·0 millivolt for full-scale deflection and time-constant 1·25 seconds for full-scale deflection. The circuit arrangements are shown in Figure 3. Chart speeds of 30–60 cm. per hour are most convenient for obstetric work.

CALIBRATION

The instrument has a pressure-sensitive part of known area. In the instrument described it is 5 sq. cm. Calibration is effected by inverting the tocometer head and resting a known weight upon the sensitive area. If, for example, 100 g. produces a recording of a 10 cm. height the instrument sensitivity is the pressure per unit area $\frac{100}{5} = 20$ g./sq. cm. for 10 cm., or 2 g./sq. cm./cm. In our particular example using the standard Honeywell-Brown chart 11 inches wide the sensitivity was approximately 1 g./sq.

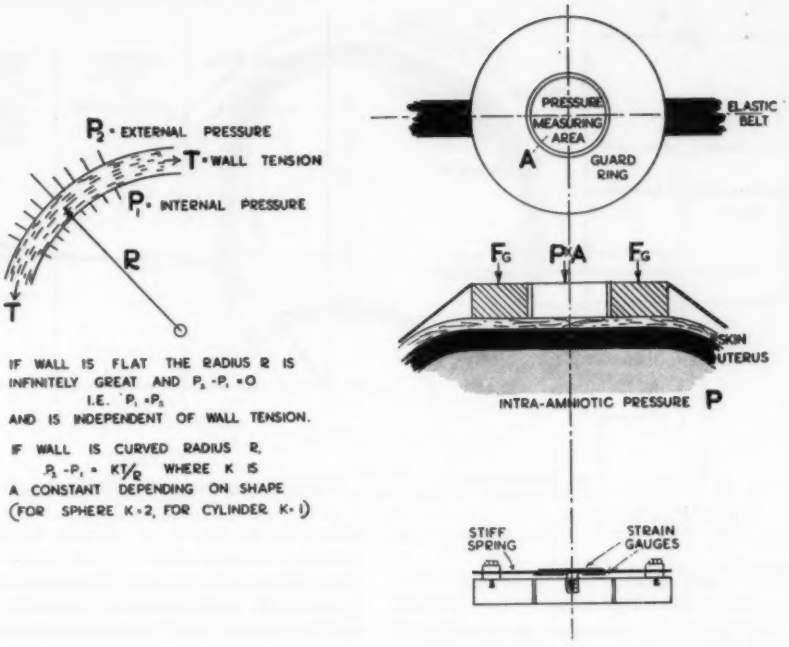


FIG. 2
Principle of Instrument.

cm./division. (The linearity of calibration is shown in Figure 4.) This calibration is exact for all patients and all uterine sites if the precautions discussed in the succeeding paragraphs are observed when applying the instrument to a patient and when interpreting the results.

APPLICATION OF THE GUARD-RING TOCODYNAMOMETER TO THE PATIENT

The instrument must be applied to the patient over a fluid-filled part of the uterus and can be held in position by hand or by a stiff elastic belt passed around the patient. The pressure of application must be sufficient to flatten the abdominal surface into contact with the guard-ring. The change in uterine volume due to this small flattening action is negligible and will not appreciably affect the intra-amniotic pressure. If the area of the tocometer is 40 sq. cm. a force of about a kilogram is sufficient but full contact may be lost at the peak of very strong contractions. If so, it may be held by hand for an exact measurement and left loosely applied for long term recordings, as too tight a band becomes uncomfortable after a while and tends to restrict uterine forward rotation. Even when loosely applied the instrument registers an approximately correct pressure. It is noted in applying the instrument, that, as the pressure of application is increased, the registered pressure increases at first then reaches a plateau where changes in application pressure do not affect the reading—this is the correct application—then if the instrument is pressed harder still it begins to affect the intra-uterine pressure and the measured pressure follows this further increase (see Fig. 5).

The tocodynamometer has a handle 5 cm. high slotted at the top to locate the elastic belt which passes around the patient. The handle

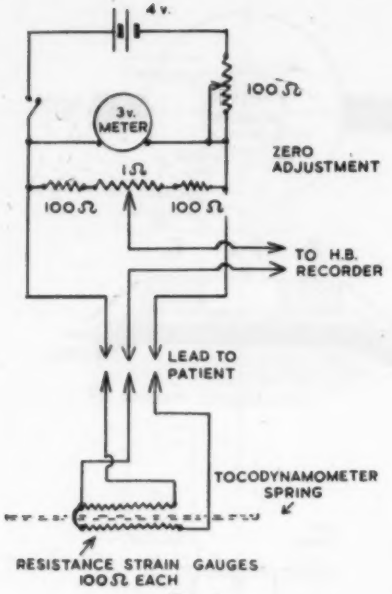


FIG. 3

Circuit for connexion to Honeywell-Brown Recorder.

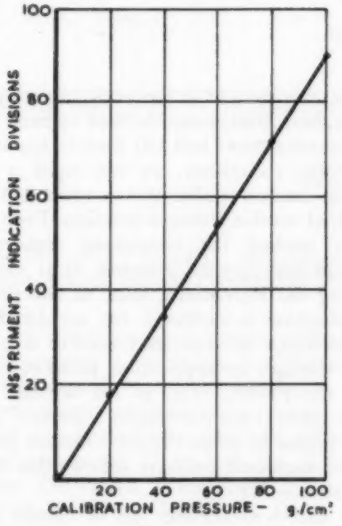


FIG. 4

Calibration.

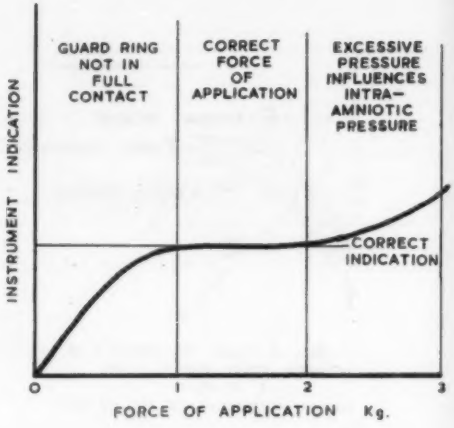


FIG. 5

Relation of pressure of application to calibration.

raises the elastic at an oblique angle and this provides a component of force centrally toward the patient and secures the gauge in position. It would be quite incorrect to attach the gauge to the patient locally with scotch tape, for it would then only measure the force required to lift the abdominal wall off the uterus.

The siting of the gauge over a fluid-filled part of the uterus, avoiding foetal back and breech, is all important, and the same pressure will be recorded no matter where the site is chosen if a suitable correction is made for gravity increasing the pressure in proportion to the height of fluid above the gauge.

If the instrument is sited in the flank, not over the uterus but over the abdominal cavity, then it will read intra-abdominal pressure. Two tocodynamometers connected in opposition, one reading intra-abdominal and the other reading intra-uterine pressures, give a combined output measuring true uterine effort, because the intra-amniotic pressure is due to uterine muscle tone added to intra-abdominal pressure (see Fig. 6). Alvarez and Caldeyro (1950) used the bladder pressure as a measure of intra-abdominal pressure.

It will be appreciated that, if the instrument is placed over a part of the uterus where the uterine wall is in contact with the foetus, the

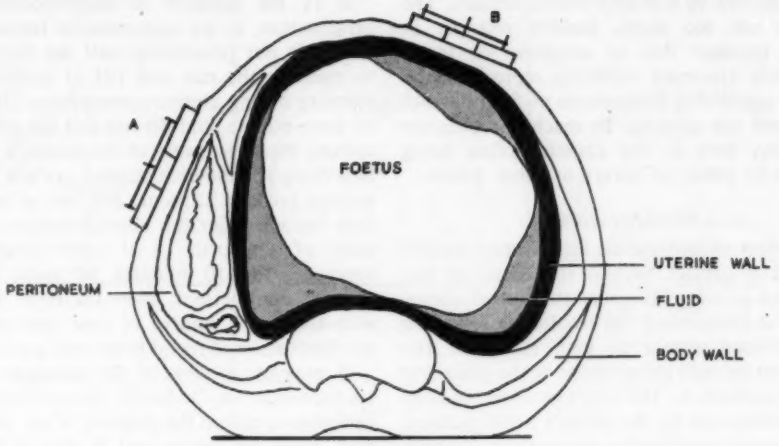


FIG. 6

Two Tocodynamometers in use to eliminate intra-abdominal pressure. An Instrument placed at A reads intra-abdominal pressure; at B intra-uterine pressure. A and B connected in opposition to recorder indicate uterine action.

registered pressure will exceed intra-amniotic pressure (otherwise there would be fluid there). The pressure recorded will be some measure of foetal turgidity and stiffness and will be difficult to interpret although pressure variations will occur which are synchronous with uterine contractions.

If there is very little or no amniotic fluid, or more especially if the membranes are ruptured effectively then the contracting uterus will become tense around the foetus without causing an increase in intra-amniotic pressure. If the gauge in such cases is placed over an unsupported part of the uterine wall it will record zero pressure all the time, i.e., the true amniotic pressure.

Figure 7 shows examples from recordings of uterine action made simultaneously with the

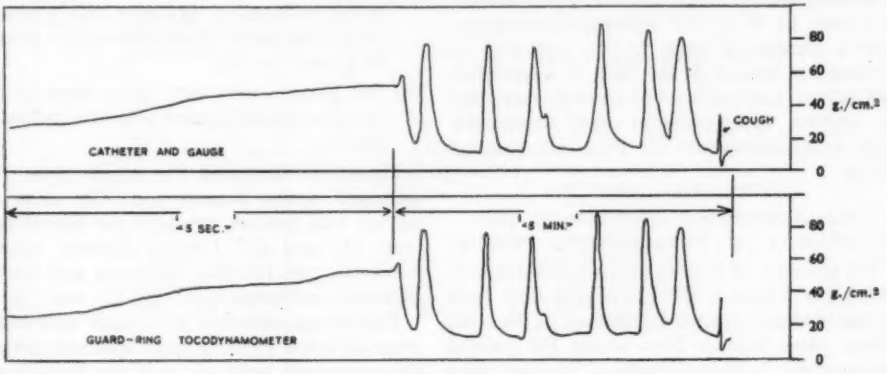


FIG. 7

Simultaneous internal and external recordings.

new gauge and by amniotic catheterization. The readings are the same. Sudden changes in internal pressure due to coughing or foetal movements are more faithfully reproduced by the new guard-ring instruments as fluid has not to traverse the catheter to reach the pressure transducer, flow in the catheter often being impeded by pieces of vernix or other debris.

Hydrostatics

The effect of hydrostatic forces upon uterine action is a subject beyond the scope of this paper, but in using the guard-ring tocodynamometer and interpreting the results the following considerations should be kept in mind. The instrument records the pressure at the place and level of application. The base line of its readings will be influenced by the posture of the patient.

Hydrostatic equalization of pressures operates in patients where there is sufficient fluid to prevent the uterine walls reaching the foetal surface everywhere. During contractions the fluid acts to make the uterus more spherical and —providing the foetal head does not completely obstruct the pelvic brim—tends to distend the lower segment. The forewaters may fill the presenting membranes and distend the cervix. The hydrostatic tone of the uterus measured in a supine patient at umbilical level is about 15 g./cm.^{2}. The cervix is some 12 cm. lower and the pressure there some 12 g./cm.^{2} greater. In the erect patient the hydrostatic pressure at the cervix may exceed fundal pressure by 30 g./cm.^{2}, so it may be 45 g./cm.^{2} between contractions. Such a pressure is equal to that sustained by a recumbent patient at the peak of a moderate contraction. Comparisons of pressure measured by uterine catheterization and tocography must make allowances for these gravitational effects.

Measurements Supplementary to the Measurement of Intra-Amniotic Pressure

The presence of frequent uterine contractions during parturition is so general that they must be regarded as a normal component of the birth forces. Most labours have about 100 painful contractions. A large number of so-called long labours are due to the cessation of contractions for considerable periods of time.

If in the absence of disproportion, malpresentation, or an unmouldable foetal head a labour is not proceeding well the first duty is to measure the rise and fall of intra-amniotic pressure during uterine contractions. (If there is no intra-uterine fluid the rise and fall of pressure around the softer parts of the foetus is the next best thing.) If the contractions are not frequent enough (at least 12/hour) and not as intense as they become after the administration of a test dose of Oxytocin (0·01 unit/minute intravenously, for 10 minutes or until the first "good" contraction), then Oxytocin infusions with tocograph control of tone and recordings or observation of foetal heart rate are helpful.

If progress is slow in the presence of good spontaneous or induced contractions it is desirable to record the pressure of the presenting part upon the cervix and if this is less than amniotic pressure suitable treatment should be instituted. This treatment has been discussed elsewhere (Ingelman-Sundberg, Lindgren and Ljungström, 1953; Smyth, 1954; Lindgren, 1955; Nixon and Smyth, 1956).

Errors in Common Types of Tocodynamometer

Tocodynamometers may be divided ideally into three categories:

(1) Those which press firmly upon the uterus and have a plunger which indents the surface.

(2) Those which follow the uterine contour and record changes of curvature with a plunger which rests upon the surface with a force of 50 g./cm.^{2} or less.

(3) Flat plates which for a given force make a variable area of contact with the abdominal wall.

Figure 8 illustrates the three types. The principal errors present are: the skin and uterine wall tension influence the recording in types (1) and (2). Uterine forward rotation influences type (2). Skin thickness and bending of tissues influences types (1), (2) and (3).

Recordings obtained with such instruments show different patterns from different parts of the uterus and weak areas of uterine wall may show the most marked contractility (Halliday, 1954). They may be useful clinically but they all

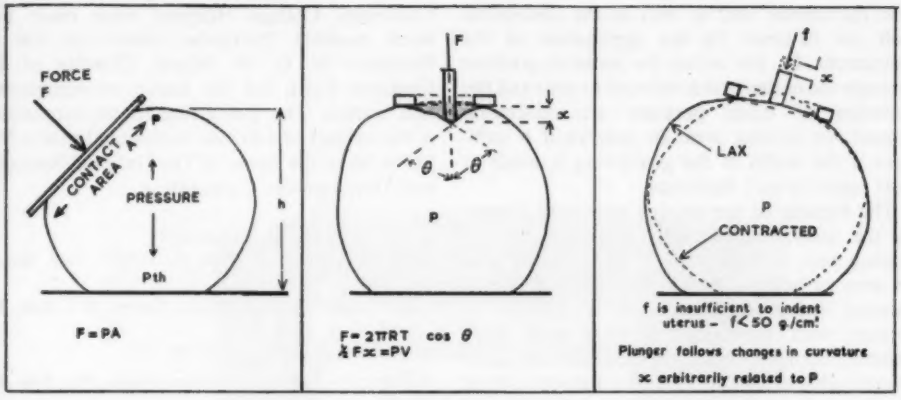


FIG. 8
Other types of Tocodynamometer.

are inconsistent between patients in the measurement of intra-amniotic pressure.

SOURCES OF ERROR IN GUARD-RING TOCODYNAMOMETER

The errors which are possible with this instrument are two-fold. Those due to imperfect design or construction and those due to its incorrect application to the abdominal wall. The latter have been fully dealt with in the text and will not arise in practice if the instructions are followed and the results correctly interpreted with regard to foetal position, posture of patient, and the level of the dynamometer with respect to the uppermost part of the uterus, subtracting the intra-abdominal pressure when necessary. In the design of the instrument the guard-ring must be made large enough to ensure

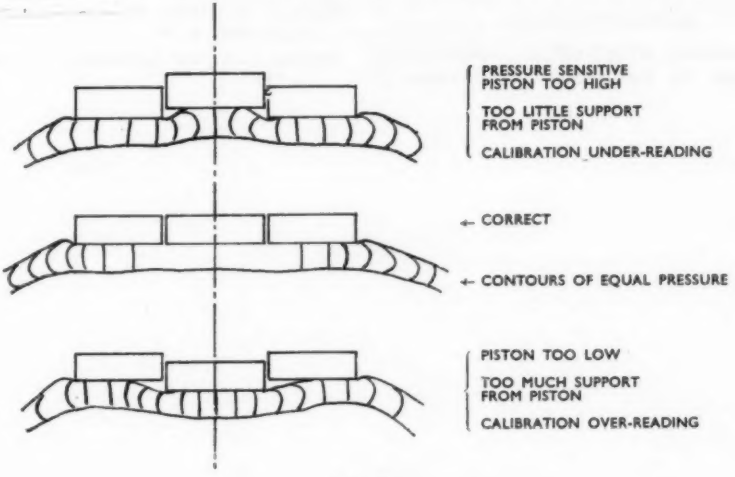


FIG. 9
Possible errors in the guard-ring Instrument.

that the uterine wall as well as the abdominal wall are flattened by the application of the instrument. By this action the pressure gradient through the entire wall is reduced to zero and the contours of equal pressure are concentric around the sensing area. In practice it is sufficient if the width of the guard-ring is made at least equal to wall thickness.

The flatness of the sensing area with respect to the guard-ring is very important. If the sensing area is forward it supports more than its area of body wall (see Fig. 9), and if it is recessed below the guard-ring it will be in contact with less area of body wall. Such defects, coupled with skin tension, will introduce considerable error. In practice a flatness $\pm 0{\cdot}02$ cm. has been found both practicable and sufficient.

Conclusions

A new type of tocodynamometer called the Guard-Ring Tocodynamometer has been described. It measures intra-amniotic pressure accurately ($\pm$ 1 cm. water) through even a thick abdominal wall, and can be applied over the patient's clothes or bed-clothes. It has applications also to measurements of intra-abdominal pressures in disease and to the study of fluid pressures in the limbs.

Acknowledgments

The generosity of the Nuffield Foundation and the support of the Board of Govenors of University College Hospital have made this work possible. Particular thanks are due to Professor W. C. W. Nixon, Director of the Obstetric Unit, for his active encouragement and advice. The guard-ring tocodynamometer is the subject of a British provisional patent No. 33354/56 in the name of The National Research and Development Corporation.

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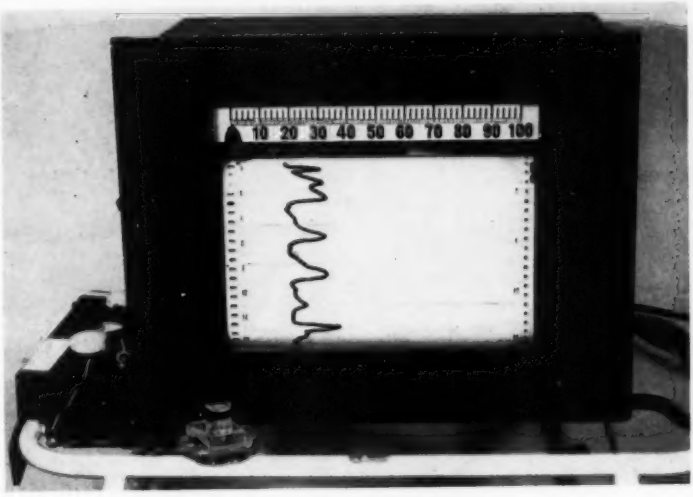

FIG. 10
Tocodynamometer and Recorder.

ECLAMPSIA—CHANGES IN PATTERN

A Commentary on a New Zealand Investigation

BY

T. F. CORKILL, *M.C.*, M.D., F.R.C.P.E., F.R.C.O.G.

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THE report of the Obstetrical Research Committee of the New Zealand Medical Research Council for the years 1954 and 1955 (1956) has drawn attention to some further significant changes in the pattern of eclampsia as it occurs today which are perhaps not fully appreciated. In the most recent editions of two at least of the leading textbooks from Great Britain, for instance, the writers are still basing some of their conclusions on the findings of the collective investigation summarized by Eden (1922), which, though accurately reflecting the position as it was in the years under review, must, in the light of this New Zealand clinical research, be regarded as completely outdated.

New Zealand has had the very great advantage of compulsory eclampsia notification for the past 30 years. Following notification, a fuller, voluntary report is submitted to the Obstetrical Research Committee by the doctor or hospital concerned. These records are used solely for scientific research and nearly 100 per cent co-operation is given by all practitioners. Over the years some 2,000 records have been collected which have provided the material for periodic surveys (Jamieson, 1931; Corkill, 1948, 1954; New Zealand Obstetrical Research Committee, 1952, 1953, 1954, 1956). By this means the progress of eclampsia control has been kept constantly before all those practising midwifery.

It may be of some interest, therefore, to summarize this experience and note some of the changes by comparison with the 1911–1922 investigation.

INCIDENCE AND MATERNAL MORTALITY

The 1922 investigators were unable to give any accurate figures for the incidence of eclampsia for the whole country but gave the maternal mortality in the 2,005 cases examined

TABLE I

Eclampsia—New Zealand

Incidence and Maternal Mortality, 1928–1955

Period	Total Births	Eclampsia Incidence	Maternal Deaths	Maternal Mortality Rate Per cent
1928–1933	157,264	491 3·2 per 1,000	93 0·61 per 1,000	18·9
1934–1939	182,069	466 2·5 per 1,000	75 0·41 per 1,000	16·1
1940–1947	334,402	466 1·39 per 1,000	67 0·20 per 1,000	14·4
1950–1952	153,191	229 1·50 per 1,000	9 0·06 per 1,000	3·9
1953–1955	164,629	206 1·25 per 1,000	5 0·03 per 1,000	2·4
1955	56,564	58 1·02 per 1,000	1 0·02 per 1,000	1·7

as 22·5 per cent—37 per cent in "severe" cases and 7 per cent in "mild" cases.

Assuming 22·5 per cent as the average maternal mortality over the whole of England and Wales at that period, a rough approximation of the incidence can be obtained. In the year 1918, for instance, there were 662,661 live births with 372 eclampsia deaths (see Table III below). On the basis of a maternal mortality of 22·5 per cent this would give an eclampsia incidence of 1,609 cases or 2·43 per 1,000 live births.

Table I summarizes the New Zealand experience in respect of incidence and maternal mortality.

Table II gives such comparable figures for England and Wales as are available (Annual Reports of the Registrar-General for England and Wales).

TABLE II
Eclampsia—England and Wales
Maternal Deaths, 1928–1954

Period	Live Births	Eclampsia Deaths
1928–1933	3,779,446	1,512 0·40 per 1,000
1936–1939	2,456,405	915 0·37 per 1,000
1940–1947	5,638,208	1,346 0·23 per 1,000
1950–1952	2,048,264	270 0·13 per 1,000
1953–1954	1,358,023	142 0·10 per 1,000

Table III gives a more detailed record of the figures for England and Wales.

Infant Mortality

Eden gave the infant mortality in the cases under review in 1922 as 46 per cent in London and 56·4 per cent in the North of England.

In New Zealand infant mortality has fallen from 42 per cent in the period 1928–33 to 16·7 in the years 1953–55. In the last year of the survey (1955) it was down to 13·6 per cent.

General Decline in Severity

The decline in severity of eclampsia in general is further indicated by the fact that there has been a steady increase in the number of cases classified as "very mild"—i.e., with survival of

TABLE III
Eclampsia—England and Wales
Maternal Deaths, 1918–1954

Year	Live Births	Eclampsia Deaths	Deaths per 1,000 Live Births
1918	662,661	372	0·56
1926	694,563	295	0·42
1936	605,292	243	0·40
1938	621,204	210	0·34
1939	619,352	220	0·36
1945	679,937	156	0·23
1946	820,719	170	0·20
1947	881,026	152	0·17
1948	775,306	115	0·15
1949	730,518	91	0·12
1950	697,000	110	0·16
1951	677,529	88	0·13
1952	673,735	72	0·11
1953	684,372	80	0·11
1954	673,651	62	0·09

both mother and infant and with fits no more than 3. In the first period, 1928–33, the incidence of such cases amounted to 16 per cent. In the last six years, 63 per cent have been of this very mild type.

Time of Onset and Relative Mortalities

The pattern of eclampsia has also changed completely in respect of time of onset and relative mortalities as will be seen by a comparison of Tables IV and V.

TABLE IV
Eclampsia—Great Britain, 1911–1922
Time of Onset and Relative Mortalities

Type	Proportion of Cases (Per cent)	Maternal Deaths (Per cent)
Ante-partum	64	20·5
Intra-partum	19	16·6
Post-partum	17	27·6

Further, of the 32 per cent of intra-partum cases the great majority had the first seizure late in labour, frequently in late second stage.

This "shift to the right" is considered to be of the utmost significance.

(1) It undoubtedly indicates that some 60 per cent of all cases (late intra-partum and post-partum) were so mild in character that the

TABLE V
Eclampsia—New Zealand, 1950–1955
Time of Onset and Relative Mortalities

Type	Number	Maternal Deaths	Infant Deaths	Very Mild Cases*
Ante-partum	136 (32 per cent)	9 (6·6 per cent)	61 (45·0 per cent)	50 (36·7 per cent)
Intra-partum	138 (32 per cent)	2 (1·5 per cent)	16 (11·6 per cent)	102 (74·0 per cent)
Post-partum	151 (36 per cent)	3 (2·0 per cent)	8 (5·3 per cent)	122 (81 per cent)

* Mother and infant surviving and no more than three fits.

threshold of eclamptic sensitivity was only reached towards the termination of labour and then only for a very short period. These cases just fell short of complete eclampsia prevention.

(2) It has meant that in this major proportion of all cases the obstetrical management presented very little difficulty. At the very most, a simple instrumental delivery was possible either immediately or within a very short time.

(3) It has meant that in all these cases the baby has been subjected to a minimum of sedative effect.

THE PREMATURITY PROBLEM

In the 1922 survey Eden found that the proportion of cases occurring at or before the 36th week varied from 22 per cent in Edinburgh to 44 per cent in London. Although the maternal mortality was only slightly higher (24·0 per cent in cases occurring before the 36th week compared with 19·3 per cent at or after the 36th week), the very great significance of prematurity in relation to infant mortality was stressed, taking into consideration all the factors concerned—the prematurity itself, effects of the disease, increased susceptibility to narcotic drugs and obstetric manipulations. Although no actual figures were given, it is obvious that, with a total infant mortality of nearly 50 per cent, the rate in the premature period must have been extremely high.

Prematurity remains the dark spot in the eclamptic picture. In the years 1950–1955 in New Zealand, 96 of the 435 cases of eclampsia (22 per cent) occurred in the 36th week or earlier. Prematurity is still the outstanding infant "killer". These 96 cases contributed 52 of the infant deaths (31 stillbirths and 21 neonatal deaths) out of a total of 85 deaths (52 stillbirths and 33 neonatal deaths) in the whole series of 435 cases.

It is true that even here the maternal mortality has been greatly reduced—to 6·2 per cent—but nevertheless this is more than twice the rate recorded for the rest of the cases (2·4 per cent). In other respects, too, this premature group presented specially serious features. The average blood pressure level was much higher—in 58 out of the 96 cases blood pressures ranging between 170/100 mm. and 230/130 mm. were recorded, the average number of fits was greater and it was considered necessary to deliver by Caesarean section in 22 cases while this was called for in only 26 of the remainder. These facts are summarized in Table VI.

TABLE VI
Eclampsia—New Zealand, 1950–1955
Period of Gestation

	36th Week or Earlier	After 36th Week
Number of cases	96 (22·0)	339 (78·0)
Maternal deaths	6 (6·2)	8 (2·4)
Infant deaths	52 (54·0)	33 (9·7)
Very mild cases (as above)	28 (29·2)	246 (72·5)
Caesarean section	22 (23·0)	26 (7·7)

(Percentages in parentheses)

This indeed, is the one disappointing feature of an otherwise very encouraging record and must focus even closer attention on this premature problem. A study of the reports reveals that in this group there was, by comparison with the rest, a much greater proportion of cases in which the antenatal care must come under criticism, particularly on the grounds that supervision was not close enough, that known hypertension was regarded too lightly or that

action was too long delayed in the face of ominous signs. Having said this, however, it must be conceded that, in the present state of our knowledge, as long as women with a hypertensive tendency, either recognized or potential, continue to have pregnancies, a considerable number of them will inevitably tend to develop super-added toxaemia at this critical early period and while, as has been shown, the risk to the mother has been considerably reduced, the correct treatment frequently calls for termination of the pregnancy and the attendant risks of prematurity for the baby cannot be avoided.

Progress in the trial of hypotensive drugs in the hypertensive toxaemias of pregnancy is being anxiously watched, for, should it prove possible with safety to the mother to prolong the pregnancy for a few weeks in a considerable number of these cases by the short term use of these drugs, this would appear to offer the best prospect of improvement in this difficult group.

Caesarean Section in Treatment

By the time of the 1922 investigation opinion was very definitely hardening against the extensive use of Caesarean section as then practised in some quarters. That summary showed a much higher mortality rate for Caesarean section, both in "mild cases" and "severe" cases, than for conservative methods.

This opinion was reflected in a very low incidence of Caesarean section in New Zealand in the years 1928 to 1939.

Then, with a safer operation, the protection of antibiotics and better selection of cases, Caesarean section once again came into greater favour and the incidence rose to about 20 per cent with results that could hardly be criticized. The decision to deliver by Caesarean section was usually made under the following circumstances:

(1) In the case where fits had been controlled but labour had not commenced and the symptoms and signs, especially hypertension, suggested urgency.
(2) In the case which did not respond quickly to sedation and in which, even though labour had commenced, the cervix was unready and resistant.
(3) Occasionally in the case with associated complications.

It was recognized that there was no place for Caesarean section as a last desperate measure in cases which were rapidly deteriorating. Fortunately, such cases were very rare.

Today it would appear that the use of Caesarean section is guided by these same considerations, but, with the increasing success of preventive measures and the general reduction in severity of eclampsia, these circumstances are occurring much less frequently. As has been shown, the incidence of Caesarean section was very much higher in the premature group, a fact which is, of course, in keeping with the indications outlined. The figures for the last 6 years are shown in Table VII.

Table VII
Eclampsia—New Zealand, 1950–1955
Incidence of Caesarean Section

Year	Cases of Eclampsia	Caesarean Section	Maternal Deaths	Infant Deaths
1950 ..	70	11	0	2
1951 ..	77	7	0	1
1952 ..	82	10	0	3
1953 ..	81	10	1	1
1954 ..	67	5	0	1
1955 ..	58	5	1	2
Total	435	48	2	10

Changes in the Whole Toxaemia Pattern

Finally this study has brought to light a most striking change in the pattern of toxaemia as a whole. The eclamptic state, *per se*, was not the outstanding feature of any of the 14 fatal cases occurring during the 6 years, 1950 to 1955. Two of them had 1 fit only, 4 had 2 fits, 3 had 3 fits, 1 had 4 fits and 1 had 11 fits.

The principal causes of death appeared to be massive cerebral haemorrhage (5), sudden cardiac failure (toxic myocarditis, 5) and the accidental haemorrhage—anuria syndrome (4).

There was not a single instance of the type of case—previously quite common—where convulsions persisted uncontrolled and led to gradual exhaustion with coma, hyperpyrexia and frequently pulmonary oedema. It would indeed

be correct to say that in this more recent experience eclampsia was no longer the most dreaded feature in a toxaemia sequence, but rather an incidental occurrence in a case where the main risk lay in acute hypertensive accidents.

This changing pattern in the toxaemia picture is further indicated by the fact that, whereas in the 6-year period, 1928–1933, cases with eclamptic features contributed 93 out of a total of 198 toxaemia deaths (47 per cent), in the last 3 years, 1953–1955, in a very similar total of births, eclampsia cases contributed only 5 deaths out of a total of 29 toxaemia deaths (17 per cent).

This trend is more fully shown in Table VIII.

This table shows a most encouraging reduction in all toxaemias but the point of particular interest is that, while the eclampsia death rate has been reduced to one-twentieth of what it was in 1928–33, deaths from the other toxaemias were only reduced to a little less than one-quarter of their earlier figure.

In summary, therefore, it can be stated that, not only has the death rate in cases with eclamptic features been tremendously reduced, but, furthermore, in the few cases where death has occurred the eclamptic element has been completely overshadowed by an acute cardiovascular incident.

A study of the toxaemia records also shows that deaths from hyperemesis gravidarum and the "acute yellow atrophy" group, which contributed substantially to the total figure in 1928–33, have also been reduced almost to vanishing point.

Stated in another way, hypertension is the most resistant feature of the toxaemia problem while the other aspects of the varying toxaemia syndrome have proved much more amenable to control.

The next table (Table IX) shows the comparable figures for England and Wales.

Very similar trends are to be noted.

Actually, in the earlier periods the death rates for all toxaemias and for eclampsia alone were considerably higher in New Zealand than in England and Wales. Up to 1940, in both instances, progress was disappointingly slow. Since then most striking advances have occurred in both countries and a very similar low figure has been achieved for all toxaemias. The New Zealand eclampsia figures however are outstanding. This is where the sustained national campaign has paid the most handsome dividends.

Summary

This record summarizes the findings of a Dominion-wide investigation of eclampsia over a period of nearly 30 years, made possible by general notification of eclampsia in New Zealand. Parallel with this there has been a sustained effort in prevention carried out by the whole maternity service.

The study indicates very striking reductions in incidence, from 3·2 per 1,000 births to 1·02 per 1,000; in maternal mortality rate, from 18·9

Table VIII

Toxaemia Deaths—New Zealand, 1928–1955

Period	Total Births	Total Toxaemia Deaths	Eclampsia	Others
1928–33	157,264	198 1·26 per 1,000	93 0·61 per 1,000	105 0·65 per 1,000
1934–39	182,069	188 1·03 per 1,000	75 0·41 per 1,000	103 0·62 per 1,000
1940–47	334,402	193 0·57 per 1,000	67 0·20 per 1,000	126 0·37 per 1,000
1950–52	153,191	38 0·25 per 1,000	9 0·06 per 1,000	29 0·19 per 1,000
1953–55	164,629	29 0·18 per 1,000	5 0·03 per 1,000	24 0·15 per 1,000
1955	56,564	2	1	1

TABLE IX
Toxaemia Deaths—England and Wales, 1928–1954

Period	Live Births	Total Toxaemia Deaths	Eclampsia	Others
1928–33	3,779,446	3,267 0·87 per 1,000	1,512 0·40 per 1,000	1,755 0·47 per 1,000
1936–39	2,456,405	1,912 0·78 per 1,000	915 0·37 per 1,000	997 0·41 per 1,000
1940–47	5,638,208	2,884 0·51 per 1,000	1,346 0·23 per 1,000	1,538 0·28 per 1,000
1950–52	2,048,264	490 0·24 per 1,000	270 0·13 per 1,000	220 0·11 per 1,000
1953–54	1,358,023	290 0·21 per 1,000	142 0·10 per 1,000	148 0·11 per 1,000

per cent to 1·7 per cent; in maternal deaths, from 0·6 per 1,000 total births to 0·03 per 1,000; and in infant mortality rate, from 42 per cent to 13·6 per cent.

Where possible, comparable tables have been given for England and Wales.

Reduction in severity is further shown by the fact that in the last 6 years, 1950–1955, 63 per cent of the cases were of extremely mild type with survival of both mother and infant and no more than 3 fits, whereas in the first period, 1928–1933, only 16 per cent of the cases were in this category.

A very important change in the pattern of eclampsia is the ever-increasing proportion of cases now occurring in the late second stage or early post-partum period where, in the main, they are of very mild type and quickly amenable to control by relatively simple measures.

Another remarkable change in the pattern of toxaemia as a whole is the very much greater proportional reduction of eclampsia deaths by comparison with other toxaemia deaths which are of a more purely hypertensive type. In more recent years, even in those cases of eclampsia which did prove fatal, the eclamptic element was completely overshadowed by acute cardio-vascular incidents.

These facts are surely a complete vindication of the value of antenatal care even in our present state of incomplete knowledge of causation. For without question these results were essentially due to preventive measures carried out with care and conviction by the majority of the doctors throughout the country. Since, in New Zealand, the maternity service is based on almost universal doctor attendance, the general practitioner-obstetrician has played a notable part in this achievement.

Certainly there have also been considerable advances in the treatment of active eclampsia but the striking thing in reading these reports is the relatively small part which such treatment has been called upon to play.

The premature group, with onset of eclampsia at 36 weeks or earlier, remains the most disappointing feature. Even in the most recent 6-year period it constituted 22 per cent of all cases and contributed 43 per cent of the total maternal deaths and 61 per cent of the total infant deaths. The difficulties of this problem and the possibilities of improvement are discussed.

ACKNOWLEDGMENTS

In this matter the writer is the recorder of the results of an investigation and a sustained effort in prevention which has been contributed to by many.

He would first pay tribute to the New Zealand Obstetrical and Gynaecological Society which, with the Department of Health, sponsored the campaign in the earlier stages and to all the doctors who by their co-operation and interest have made it possible.

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THE MANAGEMENT OF ECLAMPSIA

BY

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DURING the years from 1944 to October, 1954, 701 cases of eclampsia were admitted at the Chittaranjan Seva Sadan College of Obstetrics and Gynaecology with an overall maternal mortality of 19·0 per cent, the range varying from 12·2 per cent to 35·6 per cent (Table I). During the whole period, the conservative lines of treatment based on the technique of Stroganoff were followed. Not being satisfied with our results, we were on the lookout for a new technique. We closely followed the recent developments in the treatment of eclampsia but were not convinced by any particular technique because of the contradictory results (Browne, 1950; Menon, 1953; Morris, 1954; Stern and Burnett, 1954).

Being aware of the favourable results of a few isolated cases of eclampsia treated by artificial hibernation (Aoustin, 1953; Baccaglini, 1953), we made a pilot experiment with 46 consecutive cases of eclampsia treated with Largactil, a commercial preparation of Chlorpromazine; there was one maternal death (Mitra and Das Gupta, 1955). Being encouraged with this promising result, we pursued this new technique further and the present dissertation embodies the report of a more or less consecutive series of 133 cases of eclampsia with a mortality rate of 4·5 per cent, which has hitherto not been obtained by us.

Chlorpromazine has got a wide range of pharmacological properties affecting not only

TABLE I

Incidence with Maternal and Infant Mortality Rates at the Chittaranjan Seva Sadan from 1944 to 1954. (PP) and (UD) Indicate Post-partum and Undelivered Eclampsia Cases Respectively

Year	Total No.	PP	UD	Maternal Mortality		Infant Mortality	
					Per cent		Per cent
1944	53	11	6	11	(20·8)	36/19	(52·8)
1945	58	12	7	14	(24)	39/25	(64·1)
1946	62	12	8	14	(22·6)	42/24	(57·1)
1947	65	12	14	10	(15·4)	39/21	(53·8)
1948	56	8	1	11	(19·6)	47/28	(59·6)
1949	63	10	3	14	(22·2)	50/23	(46)
1950	88	11	12	13	(14·8)	65/41	(63)
1951	73	9	6	10	(13·7)	58/30	(51·7)
1952	64	9	3	11	(17·2)	52/29	(55·8)
1953	74	10	3	9	(12·2)	61/43	(70·4)
1954 April to 12th Oct. ..	45	6	2	16	(35·6)	37/22	(59·4)
Total	701			133	(19·0)		(58·0)

the central but also the autonomic nervous system. It potentiates the action of anaesthetic, hypnotic and analgesic drugs, thus producing a state of somnolence. This and other neurophysiological findings suggest that Chlorpromazine acts by a suppression of the awakening upward discharge from the ascending reticular formation.

Technique

1. At 0 hour: 12·5 mg. Largactil and 12·5 mg. Phenergan intravenously.
   In case of a sudden fall of blood pressure and/or acceleration of the pulse rate, 5 to 10 per cent intravenous glucose drip not exceeding one and a half litres in 24 hours.

   At the end of:
   - 1st hour: 25 mg. Largactil intramuscularly.
   - 2nd hour: 50 ml. of 50 per cent glucose solution with 5 ml. of 10 per cent calcium gluconate intravenously.
   - 4th hour: 25 mg. Largactil and 25 mg. Phenergan intramuscularly.
   - 8th hour: 25 mg. Largactil intramuscularly.
   - 13th hour: 25 mg. Largactil and 25 mg. Phenergan intramuscularly.
   - 19th hour: 25 mg. Largactil intramuscularly.
2. Continuous oxygen by a BLB mask at 3 litres per minute if the patient is anaemic, cyanotic or developing pulmonary oedema.
3. Venesection in cases of repeated fits and pulmonary oedema when the blood pressure is stabilized after an initial fall.
4. Self-retaining catheter to collect urine every 4 hours.
5. Artificial rupture of membranes if the patient is in labour and the cervix is ripe and admits a finger.
6. Low forceps application, easy breech extraction to avoid additional strain; usually done under Pentothal Sodium.
7. Penicillin and Terramycin were used liberally.

The routine scheme of treatment has been scheduled above. There were individual variations depending on the development of complications. Morphine has been practically eliminated but Pentothal Sodium was used in obstinate cases having innumerable fits. In 2 cases magnesium sulphate was administered.

To ensure uniformity of treatment one senior house surgeon was specially deputed. His special mission was to exercise constant and meticulous attention sitting by the side of the patient till the crisis was over. This was found to be the most essential part of the treatment.

No Caesarean section was done in this series.

Material

During the whole period of Largactil treatment, i.e., from 13th October, 1954 to 31st December, 1955, 146 cases of eclampsia were admitted out of the total number of 10,173 labour cases, an incidence of 1·4 per cent. Ten cases were partly treated with morphine prior to admission and the Stroganoff technique was followed in these cases. Three patients were admitted in a moribund condition. Largactil treatment was confined to 133 cases, of which 117 belonged to the ante-partum and intra-partum group and 16 to the post-partum group. Ninety per cent of all the eclampsia cases admitted were unbooked.

Blood Pressure

The earliest maximum fall of blood pressure since the institution of Largactil treatment occurred within 15 minutes in 2 cases.

In one case (Reg. No. 55/2772) the blood pressure came down suddenly from 160/140 mm. of Hg to almost nil, and remained so for about 16 hours, after which it gradually rose up to 80/40 mm. of Hg on the 18th hour. Subsequently the blood pressure was maintained at about 130/90 mm. of Hg all along till recovery. In the second case (Reg. No. 55/6259), the blood pressure came down to 0 from 180/120 mm. of Hg, but it started rising almost immediately to be stabilized at 110/80 mm. of Hg in an hour's time. There was a subsequent rise up to 160/110 mm. of Hg within 24 hours which was more or less maintained till recovery.

The range of fall of systolic blood pressure during the first 24 hours of treatment was as follows:

120 to 80 mm. of Hg in 19 cases: 1 death.
79 to 40 mm. of Hg in 53 cases: 3 deaths.
39 to 10 mm. of Hg in 52 cases: 2 deaths.
No fall in 7 cases: No death.

There were 6 deaths in the whole series. There was 1 death where the maximum fall of blood pressure was 80/80 mm. Hg, but this patient was admitted with hyperpyrexia (rectal temperature 108° F.) having an initial blood pressure of 160/120 mm. Hg and 40 fits prior to admission. Besides this case, there was no death in the group having a maximum fall of blood pressure. Evidently fatal cases could not be ascribed to fall of blood pressure during treatment.

Fits

About 50 per cent of patients were admitted to the hospital having already had 5 or more fits and in 7 cases there were more than 40 fits (Table II).

Table II
Number of Fits Before the Treatment was Started

	Mortality
1 to 5 fits in 70 cases	–
6 to 10 fits in 29 cases	1
11 to 15 fits in 10 cases	1
16 to 20 fits in 3 cases	1
21 to 25 fits in 6 cases	–
26 to 30 fits in 3 cases	–
31 to 35 fits in 3 cases	1
36 to 40 fits in 2 cases	–
Above 40 fits in 3 cases	2
Status eclamptic fits in 4 cases	–

Since the institution of Largactil treatment there was no fit after admission in 30 per cent of cases (39 cases), there was a recurrence of 1 to 5 fits in 43·6 per cent (58 cases), 6 to 15 fits in 17 per cent (23 cases), 16 to 25 fits in 4·5 per cent (6 cases), 26 to 35 fits in 3 cases and over 40 fits in 4 cases of which 2 were classed as status eclampticus (Table III).

Analyzing our fatal cases, it was found that there were 3 deaths in the group having no recurrence of fits, 1 death in the group (which was incidentally the biggest group) having 1 to 5 fits, 1 death in the group with 16 to 20 fits and 1 of the 2 cases of status eclampticus having about 92 fits, the other 1 surviving. Thus it was difficult to correlate fatal cases with the frequency of fits, although there was one significant point noticed, namely that out of 6 cases having more than 35 fits previous to treatment 3 died (Table II).*

Table III
Number of Fits After the Institution of Treatment

	Mortality
Nil in 30 cases (39 per cent)	3
1 to 5 fits in 58 cases (43·6 per cent)	1
6 to 10 fits in 12 cases	–
11 to 15 fits in 11 cases	–
16 to 20 fits in 3 cases	1
21 to 25 fits in 3 cases	–
26 to 30 fits in 1 case	–
31 to 35 fits in 2 cases	–
36 to 40 fits in 0 case	–
Above 40 fits in 2 cases (1) 44 fits (2) 55 fits	
Status eclamptic fits in 2 cases	1 (92 fits)

Pulse

The initial usual pulse rate was between 110 and 130 per minute; in 7 cases it was 160 per minute. It was characteristically observed that during the Largactil treatment there was a great acceleration of pulse rate. In 6 cases of our series, the pulse rate was almost imperceptible with an average of 130 per minute, but it became stabilized in an hour's time and there was no mortality in this series. In 40 cases the pulse rate went up to 160 per minute or more but became stabilized at about 140 per minute after an hour in 60 per cent of cases while the remaining cases were stabilized during a period varying between 48 to 72 hours. There were 4 fatal cases in this series of which 1 had an initial pulse rate of 164 per minute.

* Since the work of Lennox, Gibbs and Gibbs (1939), it has been shown that fits are prone to occur in patients who show an abnormal brain pattern (cerebral dysrhythmia) on electroencephalography. Rosenbaum and Maltby (1943) found dysrhythmia only in 10 per cent of 20 non-convulsant pre-eclamptic patients.

In this connexion it may be worthwhile quoting the remarks of Macintosh (1952): "I do not believe that eclampsia is an entity, nor that the occurrence of fits in a pregnant woman gives any real indication of the gravity of that case. We have seen that among people with cerebral dysrhythmia there are some with convulsion thresholds lower than others; and a convulsion here is merely a reflection on the patient's epileptic diathesis, and not on the severity of the toxaemia precipitating the seizure."

Respiration

The initial average respiratory rate in this series was 20 to 25/minute. This rate was usually maintained during the whole course of treatment. In 2 cases the respiratory rate became irregular along with an acceleration of pulse rate to about 160 per minute, but ultimately became stabilized without any untoward result. Pulmonary oedema developed in 5 cases only of which 1 took a serious relapse with 44 fits; venesection tided over the situation. There was no mortality in the series developing pulmonary oedema.

Urinary Output

There was 1 case of anuria which proved fatal. The average urinary output in the first 24 hours was less than 300 ml. in 40 per cent of cases, between 300 ml. to 600 ml. in 40 per cent of cases and, in the remaining 20 per cent, it was above 600 ml.

Recovery

Full consciousness was regained in about 50 per cent of cases within 24 hours. The recovery started as early as 8 hours in 10 cases and as late as 72 hours in 10 cases. It took 4 days to regain full consciousness in 3 cases. In 5 fatal cases the patients never recovered consciousness.

Mental confusion and disorientation developed after recovery in 6 per cent of cases, which usually passed off in about a week's time. In one case it persisted for 31 days.

Obstetric Interference

Our school strictly adheres to the conservative line of treatment. The membranes were ruptured artificially only when the patient was in labour and the cervix was ripe. Forceps were applied under Sodium Pentothal when the head was low down in the perineum to cut short the strain of the second stage of labour in 49 cases. In 6 cases, where the foetuses were dead and the cervix was fully effaced, the head was perforated. There were 4 sets of twins.

Six cases remained undelivered during the active treatment, of which (1) one (Reg. No. 55/2813) was admitted in a low condition having had more than 40 fits outside without any treatment and died shortly after the treatment was started; (2) one (Reg. No. 55/8409) was discharged undelivered; later, after 6 weeks she was confined of a living child; (3) one (Reg. No. 55/7649) was delivered after 28 days of a living child; (4) one (Reg. No. 55/6453) was delivered after 19 days of a living child; (5) one (Reg. No. 55/7005) was delivered after 13 days of a stillbirth and (6) one (Reg. No. 55/7872) was delivered after 8 days of a stillbirth. It is thus evident that obstetric interference of the nature of Caesarean section was not indicated during the active course of treatment for eclampsia.

Results

Of 146 eclampsia cases there were 10 cases which were previously treated with morphine and which were not included in the Largactil series. Three patients were admitted in a moribund condition and died shortly after. There were altogether 13 deaths in the whole series thus having an overall mortality rate of 8·9 per cent. So far as the Largactil series was concerned, there were only 6 deaths in 133 cases thus having a mortality rate of 4·5 per cent, as compared with our average maternal mortality rate of 19·0 per cent for the last 11 years (Table I). Even the uncorrected maternal mortality rate of this series which is 8·9 per cent was significantly less than the average mortality rate in our hospital and the maternal mortality rate of the Largactil series (4·5 per cent) was definitely the least.

Analyzing the fatal cases of the Largactil series it was found that 1 died of status eclampticus, 1 of hyperpyrexia, 1 of cerebral haemorrhage, 1 of anuria, 1 of septicaemia and 1 of pulmonary embolism on the 9th postpartum day. It is remarkable that the severity of obstetric shock was least in this series. It was our bitter experience that obstetric shock used to take a heavy toll in our previous cases requiring even such ordinary obstetric manœuvres as forceps or perforation extraction. Analyzing our last 30 deaths from eclampsia prior to this series it was found that nearly 50 per cent (14 cases) died of obstetric shock within an average of 8·5 hours (range—3 hours

to 18 hours) after confinement which was mainly instrumental.

Foetal loss was also definitely less in this series. There were 45 stillbirths including 4 sets of twins. The uncorrected foetal mortality rate was 39·0 per cent against an average of 58·0 per cent of the last 11 years (Table I). If 6 perforation cases were excluded, the mortality rate would be 33·9 per cent. No foetal heart sounds could be heard on admission in 28 cases of which 23 cases had more than 10 fits prior to admission. It is presumed that heavy foetal loss would have been greatly reduced if the treatment could have been instituted immediately with the onset of eclampsia. We have, however, observed a very interesting phenomenon, namely, that live babies were born in 2 cases having 55 fits after the institution of treatment and in 1 case having 30 fits.

Summary

(1) We report 133 cases of eclampsia treated with Chlorpromazine (Largactil).

(2) There was a marked initial fall of blood pressure and acceleration of pulse rate which in general was stabilized during the course of treatment.

(3) There were 6 deaths in the series. The maternal mortality rate was 4·5 per cent. This can be favourably compared with a maternal mortality rate of 19·0 per cent in eclampsia cases in the same hospital for the last 11 years.

(4) The infant mortality rate (uncorrected) was 39 per cent, which was definitely less than the average foetal mortality (58·0 per cent) of the last 11 years.

(5) The incidence of obstetric shock was minimal.

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FENESTRATION OF THE FOETAL MEMBRANES

BY

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IT is well known that rupture of the foetal membranes is usually followed within a few hours or days by the onset of labour, and yet cases are sometimes encountered where it is delayed for many weeks or months. Juskowitz and Weinstein (1954) described a patient who was delivered 59 days after spontaneous rupture of the membranes, during which time a continuous loss of liquor occurred *per vaginam*. Putterman (1950) reported a similar interval of 87 days, Gozan (1952) one of 116 days, and Meyer-Rüegg (1904) one of 120 days. A patient was recently delivered at the West Middlesex Hospital after an interval of 63 days had elapsed between the time of spontaneous rupture of the membranes and delivery, and, as her case throws some light on the reason for this occurrence, it is thought to be worthy of reporting.

CASE REPORT

Mrs. R.M., aged 31, had 2 previous full-time pregnancies, the first in 1947, resulting in the birth of a normal 8-pound girl, and the second, in 1954, in a 7½-pound boy with a large cervical meningocele, who died after 36 hours.

She attended the antenatal clinic on 1st July, 1955, the last menstrual period being on 14th May, and the expected date of delivery on 21st February, 1956. She appeared a healthy young woman, and had a negative Wassermann reaction, blood group A, Rhesus type positive, a haemoglobin level of 12·8 g. (86 per cent Haldane), and mild hypertension of 140/90 mm. Hg. On 12th July she had slight vaginal bleeding, which recurred on 23rd, 27th and 31st July, and 3rd August. When she next attended on 10th August, at the 12th week, the uterus was the size of a 10-weeks pregnancy, and was retroverted in position lying in the hollow of the sacrum. She was admitted to hospital as a case of threatened abortion, and was treated with rest and sedation. Whilst in bed an intermittent reddish-brown discharge occurred, but the cervix appeared healthy on inspection by speculum, and there were no other diagnostic features of a hydatidiform mole or an extra-uterine pregnancy. During the succeeding weeks her uterus continued to enlarge, and, when she was discharged on 22nd September at the 18th week, her pregnancy appeared to be progressing normally, apart from the persistent mild hypertension.

When seen in the clinic on 12th and 26th October (21st and 23rd weeks) she complained of further intermittent losses of blood and brown discharge, and was advised to rest at home. On 9th November (25th week) she stated she was continuously wet, and on examination clear fluid was found to be discharging *per vaginam*. She was admitted to hospital forthwith.

On detailed questioning, she stated that on 29th October (24th week) when sitting quietly at home in a chair, she felt something "give" in the region of the left iliac fossa and a rush of "dirty brown water" occurred from the vagina. There was no bleeding. She assumed "her waters had broken". The watery loss had continued whilst she was in bed that night, and had troubled her ever since. It seemed to be greatest in quantity in the evenings.

On examination she had a normal temperature, pulse and respiration rates, and a blood pressure of 140/90 mm. Hg. The fundus of the uterus corresponded in height to a 26-weeks pregnancy, external ballottement was normal, and, although the foetal heart sounds could not be heard, the patient stated she could feel foetal movements. On speculum examination, an erosion 1 cm. in diameter was seen on the anterior lip of the cervix. Examination of high vaginal swabs showed epithelial cells only and no bacteria.

When at first in hospital she soaked about four pads per day. Micturition was normal, and the fluid loss was quite clear and non-staining, not resembling urine in any way, but having the characteristics of liquor amnii. No foetal abnormality could be seen on X-ray examination. As pregnancy advanced the foetus grew apparently normally, but the discharge of liquor became more profuse, being blood-stained at times, until by 17th December (31st week) twenty-five pads per day were necessary. The foetal heart sounds could now be heard and were normal in rate and rhythm. At 12.30 p.m. on 31st December (33rd week), when the foetus presented in the R.O.L. position, she went into labour. It was noted that the discharge became less with the onset of

labour, and this was thought to be due to the descent of the head. The first stage lasted 4 hours 55 minutes, and the second stage 8 minutes, after which a healthy female infant, weighing 4 pounds 7¼ ounces (2,017 g.) was born. No noticeable amount of liquor was lost either during or after the delivery. The placenta followed in 1 hour 45 minutes, giving a total delivery time of 6 hours 48 minutes. Blood loss amounted to 3 ounces (85 ml.). Leakage of liquor had thus occurred continuously for 9 weeks (63 days) from the time of rupture of the membranes until the delivery.

Subsequently the puerperium was normal, and, although the baby became jaundiced and at first caused some anxiety, it was able to be discharged on 3rd February, 1956 (34th day) when it was fully breast-fed, weighed 5 pounds (2,268 g.), and was gaining weight steadily.

The Placenta and Membranes

The placenta appeared normal in structure, weighing 1 pound 2 ounces (510 g.), whilst the cord was normal in attachment and 30 inches in length. Inspection of the membranes, however, revealed some features of interest. They appeared normal in size, the sac being large enough to accommodate the foetus. They were, however, not attached to the edge of the placenta, and, although there was no circumvallate formation, a large rim of placenta had protruded into the decidua bereft of a membranous covering (Fig. 1). The main site of rupture of the membranes, through which the baby had passed, could be demonstrated quite easily (Fig. 1), but 15 mm. away from its edge was a well defined elliptical hole measuring 25 mm. and 18 mm. along its axes (Figs. 1 and 2). The edge of the hole appeared regular and slightly thickened, in distinction to that of the larger hole which was irregular and thin. It would seem that the smaller hole was old-standing and was presumably the route by which the liquor had escaped *ex utero* during the 9 weeks of pregnancy, whilst the larger hole had formed during the course of labour.

Histology of Membranes

The textures of the edges of the holes were quite dissimilar when palpated, and it was thought that histological examination of the membranes bordering on the holes might reveal some essential differences. These are shown in Figures 3 and 4, and I am indebted to Dr. Counsell, Pathologist at the West Middlesex Hospital, both for their preparation and his report, as follows:

"Histologically the membrane consists of the following layers:

(1) A layer of amniotic epithelium,
(2) A layer of amniotic mesoderm fused with
(3) A layer of chorionic mesoderm,
(4) Decidua.

"Sections of the foramen which appeared during pregnancy and of the edge of the naturally ruptured membranes show striking differences. Whilst the edge of the ruptured membranes is ragged (Fig. 4), consistent with having been torn, the foramen (Fig. 3) shows a smooth rounded slightly bossed edge, covered by a thin hyaline membrane.

"It would appear that after the rupture which presumably caused the foramen a change took place resulting in rounding off of the edge. This change could scarcely be of vascular origin, the amnion being avascular. It seems probable that necrosis of the ragged projections resulted in a rounding off of the edge. The covering hyaline membrane would result from a fibrinous exudate from the edge of the membrane, there being no evidence that liquor amnii contains fibrinogen."

Differential Diagnosis

Previous writers who have discussed the cause of prolonged leakage of liquor during pregnancy have almost invariably referred to hydrorrhoea gravidarum, which they have described as a discharge from the cavity of the uterus attendant upon a decidual endometritis (De Lee and Greenhill, 1948). It is perhaps doubtful whether this exists as a clinical entity *sui generis*, and although hydrorrhoea may describe the symptom from which the patients suffer it is certainly not the diagnosis here.

Cases of early rupture of the membranes during pregnancy with reconstitution of the chorion have been described by Hückel (1936) and Meyer-Rüegg (1939). In the latter author's case an instrumental attempt to procure abortion was unsuccessfully made at the 12th week of pregnancy, when the membranes were ruptured; the loss of liquor ceased after about a week, and at the eighth month a severely deformed child was born. It is suggested that in

FIG. 1

Photograph of placenta and membranes showing site of the natural rupture and of the fenestration.

FIG. 2

Enlarged view of the fenestration.

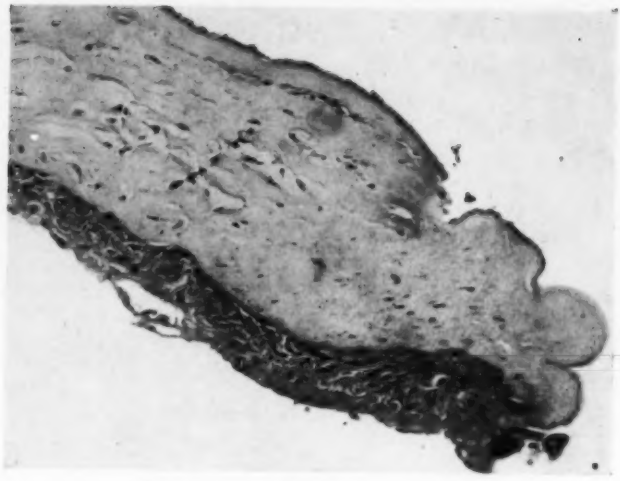

FIG. 3
Section of the edge of the fenestration. ×100.

FIG. 4
Section of the edge of the natural rupture. ×100.

this condition (which has been named graviditas examnialis), the ruptured amnion, being devoid of blood vessels, is incapable of repair, whilst the chorion, lying adjacent to the decidua, can easily repair itself. Accordingly the punctured amnion collapses towards the insertion of the cord and becomes entangled around the foetus, whilst the chorion re-grows and arrests the flow of liquor. Meyer-Rüegg stated that on detailed examination of these cases, the presence of amniotic bands (Simonart's threads), which give rise to amputations of the extremities and other deformities, can always be found. As the reconstitution of the chorion prevents prolonged drainage of liquor during pregnancy, this diagnosis is not the correct one in the present case.

One recognized cause of a continuous loss of liquor during pregnancy has been named amniotic-chorionic leakage. Schuman (1951) described 16 cases in which rupture of the membranes occurred, and was followed by a persistent leakage of liquor. During labour a second sac of membranes appeared and needed to be artificially ruptured. The maximum time this leakage occurred was 15 days. He explained this double rupture of the membranes by suggesting that liquor amnii passed by transudation or secretion into the extra-embryonic coelom between the amnion and chorion, converting it into a fluid-filled cavity. The chorion then first ruptured allowing liquor to escape from this space, and the amnion ruptured later. He stated that the two expulsions of liquor may be equal in volume, or either may be the larger.

A similar case was described by Morton (1952) in a discussion which followed a paper read by Calkins (1952) on this subject. He explained the distension of the extra-embryonic coelom by the presence of a small semilunar area situated near the insertion of the cord, which allowed the passage of the liquor through the amnion to occur. Roth (1954) reported some even more remarkable examples of this condition; in 14 patients the first rupture occurred at some time between the 28th and 38th weeks of pregnancy and the second rupture during delivery—the greatest interval of leakage being 15 weeks. In 3 patients the double rupture occurred during pregnancy at an interval of between 2 and 6 weeks, with labour ensuing in one case 6 weeks later.

In all these cases of amniotic-chorionic leakage the liquor collected between the two membranes, and their separate acts of rupture produced the observed clinical picture. In the present case there was presumably a second rupture of the amnion during labour although it was not specifically observed at that time, so that the case might superficially resemble one of amniotic-chorionic leakage; the sections of the membranes indicate, however, that the double ruptures were of both membranes and not separate ruptures of the amnion and chorion. This case cannot therefore be considered to be an example of amniotic-chorionic leakage.

Another condition known to produce a prolonged loss of liquor during pregnancy is graviditas exochorialis, or extramembranous pregnancy. Here there is rupture of both membranes during pregnancy with consequent discharge of liquor which may continue for many weeks. Siddall (1946) described a patient who discharged liquor for 13 weeks from the 18th to the 31st week of pregnancy when labour supervened. At birth the infant weighed 4 pounds 1 ounce (1,842·7 g.) and was obviously much too large to have developed within its membranous sac. Baker and Savage (1950) reported a similar case in which loss of liquor persisted for 53 days. They comment upon the facts that the loss in these cases is always painless and frequently blood-stained, that the pregnancy never reaches term, that the child is puny and shrunken, with some of its joints ankylosed, and that intra-uterine infection does not occur. The present case is not of this category, as the membranes were of normal size, the sac being quite adequate to accommodate the foetus.

The case described with the elliptical hole in the membranes does not accord with any of these diagnoses:

(*a*) It might be considered an incomplete case of graviditas examnialis in which a small rupture of the amnion occurred, sufficiently large to allow liquor to escape but no part of the foetal body. However, as liquor was lost throughout the remainder of pregnancy, there was no reconstitution of the chorion as occurs in this condition, and there were no foetal deformities.

(*b*) It cannot be regarded as a variant of amniotic-chorionic leakage since histological examination showed both membranes to be present at the edges of the perforations. On the other hand, cases previously described as being due to amniotic-chorionic leakage may in fact have resulted from a small hole appearing in the membranes during pregnancy, the presence of the foramen not having been noticed after delivery.

(*c*) Although this case had many features in common with extramembranous pregnancy, such as the blood-stained loss, the premature delivery, and the absence of infection (this was in fact the clinical diagnosis made prior to delivery), comparison of the size of the child and its membranous sac showed that this diagnosis was incorrect.

It has been suggested that this entity be termed "Fenestration of the Membranes", this being in fact a simple description of the state of the membranes found at delivery. It may occur more frequently than is commonly realized, for many authors who describe cases of prolonged loss of liquor have not subjected the foetal membranes to any close inspection, whilst in some cases no doubt the foramen becomes obscured by being torn open and incorporated into the natural rupture that takes place during labour.

Discussion

Although the route of escape of liquor amnii in this case is known, two major issues are left unsettled, namely, the manner in which the fenestration was produced, and the reason why labour did not supervene sooner. The following reasons for the cause of the occurrence may be considered:

(1) *Trauma.* It is unlikely that the membranes ruptured as a result of trauma applied *per vaginam*, for the fenestration lay some distance inside the lower segment of the uterus away from the internal os. This is indicated by the position of the foramen alongside the site of the rupture that occurred during labour (Fig. 1), and also by the fact that decidua is still adherent to the outer surface of its edge (Fig. 3). There was, moreover, no history of the passage of instruments in an attempt to procure abortion, and the time of the rupture at the 24th week of pregnancy makes this unlikely. As it did not occur during intercourse it cannot be ascribed to coital trauma.

(2) *Inherent weakness of the membranes.* This is also an unlikely cause, as Danforth, McElin and States (1953) have shown that the time of rupture of the membranes during labour is independent of their intrinsic strength, as measured by their bursting tension. This has been confirmed by Embrey (1954) who stated that rupture of the membranes in labour depends on factors other than their tensile strength. These opinions, based on the measurements of the bursting tension of the membranes obtained during labour, are probably equally applicable to pregnancy, as Danforth *et al.* found that the bursting tension of the membranes was independent of the duration of the pregnancy.

(3) *Increased intra-uterine pressure.* Williams and Stallworthy (1952) demonstrated that the basal intra-uterine pressure amounts to 8 mm. Hg, and this rises to between 40 and 90 mm. during first stage contractions. Similar figures were obtained by Caldeyro Barcia and Alvarez (1952), who found a basal tonus of 8 to 12 mm. Hg and amniotic pressures during first stage contractions rising to between 30 and 50 mm. Hg. Pain is induced when the pressure exceeds 25 mm. Hg. They also reported that the amniotic pressure during Braxton-Hicks contractions of late pregnancy rises to about 18 mm. Hg. Embrey (1954) showed that the average pressure required to cause rupture of the membranes in his experiments was $58{\cdot}9 \pm 11{\cdot}5$ mm. Hg. It is highly improbable, therefore, that in the present case, when the patient was sitting quietly in a chair, at the 24th week of pregnancy, quite free from pain, the pressure exerted by the Braxton-Hicks contractions could have caused the membranes to rupture in the absence of any other causative factor.

(4) *Extreme thinness of the membranes.* Danforth *et al.* (1953) have shown in a series of cases that the membranes vary in thickness from 152μ to 330μ, with a modal value lying between 228μ and 254μ. In the present case the thickness of the membranes, as measured with a micrometer eyepiece, was found to vary from 280μ to 350μ, with an average value of 315μ; according to Danforth's data, therefore, the thickness of

the membranes exceeds the average value, and consequently cannot be held responsible for causing the fenestration.

(5) *Infection or degeneration of the membranes.* This hypothesis is disproved by histological examination of the tissues involved, which reveals no evidence of these processes.

(6) *Congenital deformity of the membranes.* Since both amnion and chorion were absent from the site of the fenestration it would seem unlikely that a congenital abnormality was responsible, for this would not affect two membranes derived from different embryonic layers at the same site. However, as the amnion is the membrane with the greater tensile strength, it is possible that some abnormality of this structure led to loss of its continuity, the chorion subsequently giving way and enabling the fenestration to form.

(7) *Infarction of the membranes.* As the chorion is nourished by the decidua, it is possible that its integrity was impaired by disease of this structure. This may have led to an abnormal attachment of the chorion, with the result that small separations were induced by the uterine contractions, giving rise to the repeated episodes of vaginal bleeding. Later the decidual disease may have caused infarction of the adjacent portion of chorion, with subsequent rupture of the amnion at the weakened area. However, the decidua appeared quite normal on microscopic examination.

In summary it may be said that none of these reasons is convincing and the cause of the fenestration must for the present remain undetermined.

It is difficult to explain the prolongation of pregnancy for 63 days following the rupture. As there are no sudden fluctuations in the volume of the liquor during normal pregnancy, it is to be assumed that the amount of liquor formed by secretion, transudation, and micturition is approximately equal to the volume removed by swallowing. In the present case the foetus presumably swallowed less, so that the combined loss of liquor by leakage and swallowing was roughly equal to the amount being formed, and the balance enabled the pregnancy to continue. It was noted at the time that, despite the persistent leakage, the volume of liquor within the uterus appeared normal on examination, as external ballottement was the same as that obtained in normal pregnancy; also wide variations in the foetal heart rate never occurred, as might have been expected if the area of the placental site had been reduced by the excessive loss. The site of the rupture within the lower segment was presumably responsible for the slow loss of liquor, the uterine wall acting as an inefficient plug, with the consequent maintenance of an adequate volume of liquor within the uterus which allowed the pregnancy to continue for so long.

It is hoped that this case presents some new aspects relating to hydrorrhoea gravidarum and allied states, but the true solution of the problems involved still awaits further observation.

Summary

(1) The causes of prolonged loss of liquor amnii during pregnancy are discussed.

(2) A case is described in which continued leakage for 63 days was due to fenestration of the foetal membranes.

(3) Histological descriptions are given of the edge of the fenestration which appeared during pregnancy, and of the natural rupture which occurred during labour.

(4) Some suggested causes for the occurrence of the fenestration are discussed.

Acknowledgments

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SOME OBSERVATIONS ON BRENNER TUMOURS AND WALTHARD CELL NESTS

BY

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THE argument as to the relationship between Brenner tumours of the ovary, pseudomucinous cystadenomas of that organ and the Walthard cell nests which are found on it or close to it is too familiar to require detailed documentation. For the sake of completeness, however, it must be stated that the Walthard nests occur most characteristically under the peritoneum of the Fallopian tube and are thought to be derived from that membrane by metaplasia (recent references are Crome, 1950 and Teoh, 1953a). Brenner tumours of the ovary undoubtedly show nests with a transition to the pseudomucinous type of epithelium in the small cysts which arise within the Brenner cell nests while areas of Brenner tissue may sometimes be found among large pseudomucinous cystadenomas of the ovary, but it is by no means certain that they would always be found if looked for long enough. True, patient search of individual tumours has solved many of the classical problems of tumour pathogenesis, e.g., that of the nature of oat-celled tumour of the lung (Barnard, 1926) but the logical limitations of the method must be realized, i.e., that it sets out sometimes to prove a negative.

The origin of Brenner cell clumps from Walthard nests, in fact their identity, has been asserted many times but recently further evidence against the idea has been adduced by Teoh (1953b) after a detailed study of 16 Brenner tumours. He could find no consistent differences between the two types of cell nests on either cytological or histochemical grounds. His histochemical stains were used to identify fat, glycogen and mucin. However, although he found mucin in the degenerating cells surrounding the vacuoles which arise in Walthard nests, he was unable to identify columnar epithelium in them, as opposed, of course, to the Brenner nest. Glycogen he found commonly in Brenner nests but not in those of Walthard, while the Brenner nests alone were closely associated with fat-laden cells of the thecal type. This last observation in particular led him to believe that the two types of nest were not of the same origin and that the Brenner cells must be derived from the same stem as granulosa and thecal cells.

Recently a tumour came under my notice which appears to throw fresh light on the problem. It has been compared with 7 other tumours observed at this hospital during the past 6 years.

CASE REPORT

Mrs. M. was a woman of 72 years who came to the clinic complaining of irregular post-menopausal bleeding of one year's duration. Clinical examination revealed a large, irregular mass filling the pelvis and she was submitted to laparotomy. What appeared to be an irregular, solid tumour of the right ovary was found with the corresponding tube embedded in it. The mass was densely adherent to surrounding structures, including the uterus. A total hysterectomy and bilateral oöphorectomy was performed, but considerable technical difficulties were encountered and the tumour was removed in several fragments which afterwards were difficult to orientate or piece together. A considerable number of blocks were taken, but unfortunately the interesting nature of the specimen was not realized during the early stages of its examination and so only these paraffin-embedded blocks remain for detailed study. This restricts the range of histochemical tests which can be applied.

DESCRIPTION OF THE HISTOLOGY

Outside the tumour mass the endometrium and tubal mucosa call for comment. The endometrium shows marked hypertrophy with glandular dilatation, in fact the picture typical of post-menopausal hyperoestrinism. The tubal

mucosa also shows marked activity and in a younger woman would be described as in the late interval phase. Although marked activity of the tubal mucosa is not uncommon in post-menopausal women for no obvious cause (Rewell and Towers, 1956), the combination of the changes in tube and uterus makes it almost certain that the patient was subject to strong, post-menopausal, oestrogenic influences. An extraneous source was strenuously denied.

The right tube passes through the edge of the tumour and Walthard nests are seen on the peritoneal surface of the tumour adjacent to it. All of those found were partly cystic, many being only a thin shell of flattened cells. All were, however, typical (Fig. 1). In one, in addition to the main cyst, small spaces were seen in the main cell mass (Fig. 3). Although much flattened, the lining cells were well within the range seen in the definite acini found in the main tumour (*vide infra*). It is particularly noteworthy that P.A.S. and mucicarmine revealed mucin within the Walthard nests only in the cells lining the cyst and these acini. The nests overlay connective tissue which appeared to be of the usual fibrous variety and cannot be claimed as thecal.

Solid Areas of the Tumour

These were obviously of the Brenner type containing typical cell nests (Fig. 2) surrounded by a plump-celled fibrous type of tissue which may well be theca. As stated above, special stains for fat could not be applied to the material preserved. Many of the nests showed metaplasia to the pseudomucinous type of epithelium forming microscopic cysts. The cells of all these smaller nests were of a uniform pattern, apart from the fact that a larger number than usual showed vacuolation. Once more it is noteworthy that the special stain revealed mucin only in those cells on a free surface.

Cystic Areas

Some areas contained simple macroscopic cysts, up to about a cm. across. The lining epithelium of these was of great interest. Under the lowest power of the microscope it was thought to resemble a follicle cyst, but closer examination revealed what would have corresponded to the granulosa layer to consist of much more elongated cells with larger, fusiform nuclei, although a fair degree of pleomorphism was present. Many of the cells were vacuolated while the cysts were sometimes lined with unmistakable pseudomucinous epithelium. Again, many small acini of such cells were found within the thickness of the layer (Fig. 4). It was indeed evident that the nuclei of all the cells in the lining of each cyst were indistinguishable and they had only to be pushed into line with their mucin at one end for a typical pseudomucinous type of epithelium to be formed. Once again it was noteworthy that special stains revealed the presence of mucin only in those cells on a free surface.

Most interesting of all were areas in which such cyst linings were even more developed, forming a complicated papilliferous pattern. The lining epithelium presented an identical appearance, consisting of the large, elongated cells, many being cystic and with a lining of pseudomucinous epithelium and numerous small acini in the thickness of the wall in addition. The supporting stroma could well have been theca. Mucin was distributed in the same way as before and in both simple and papilliferous cysts it lay free in the lumen.

No mitosis was found in any area examined in any part of the tumour.

Discussion

There seems no doubt that the epithelium lining all the cysts of this tumour is indistinguishable histologically from that of the solid tumour nests, i.e., is Brenner epithelium. Most Brenner tumours are, of course, small and indeed most are only incidental findings. In this case the tumour would appear either to have grown more rapidly than usual or to have been allowed to go on for an unusually long time, probably the latter as no mitoses were found and it was not much distended by the mucin produced. Such distension might have made it appear to grow more rapidly than a solid mass. Apart from possible thecal cells, which constitute an essential part of a Brenner tumour anyway, no other cell types were found. There would appear to be three main themes for discussion, viz.: (*a*) the relationship of this individual tumour and of the

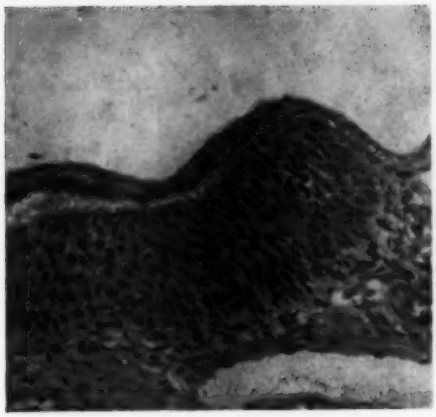

FIG. 1
Walthard nest on the surface of the Fallopian tube. ×240.

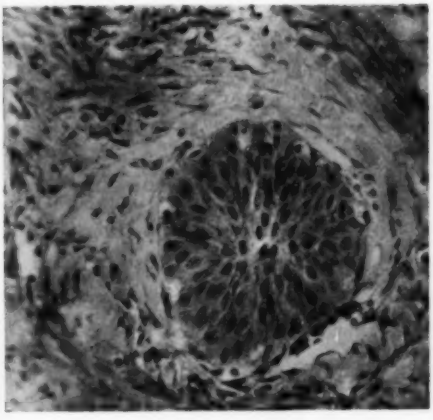

FIG. 2
Brenner cell nest within the tumour. ×240.

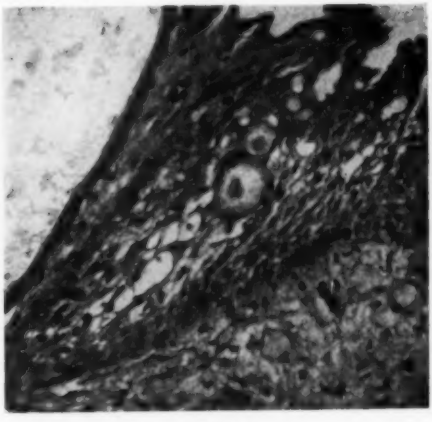

FIG. 3
Columnar epithelium in a Walthard cell nest. ×240.

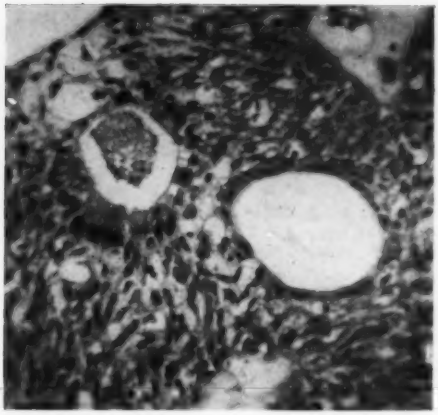

FIG. 4
Columnar epithelium in a mass of Brenner cells. ×240.

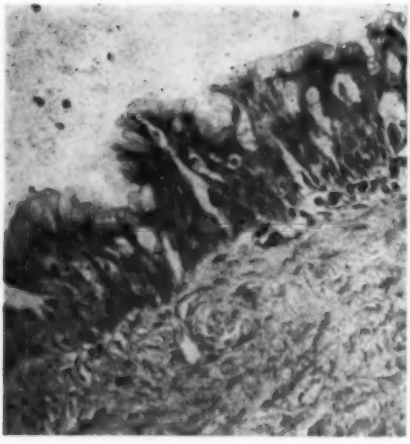

FIG. 5
Cells of the Brenner type lying beneath the mucin-bearing mucosa of a large cyst. ×240.

class in general to the pseudomucinous cystadenoma, (*b*) its relationship to the Walthard nests and (*c*) the significance of its hormonal activity.

(a) *Relationship to Pseudomucinous Cystadenomas*

From the histological point of view, it would seem possible, as stated above, that the cells of such a tumour as this, when arranged in a particular manner or pattern, would have the appearance of pseudomucinous epithelium. It is in fact legitimate to speculate that the appearance of such a mucosa is dependent on mechanical factors only and that, once mucin has accumulated in an extracellular rift, the surrounding cells might be pressed into the characteristic tall columnar shape with their intracellular secretion at their free edge.

Of the other Brenner tumours examined, two were associated with large pseudomucinous cysts. One was found in the wall of what was otherwise a typical pseudomucinous cystadenoma with a single layer of the characteristic cells lying on a basement membrane immediately above what appeared to be a stroma of simple fibrous tissue. The other, however, was somewhat more complex. It occurred in a woman aged 61 years who complained of dragging pains in the lower abdomen. As well as a prolapse she had a small ovarian cyst, which was removed and found to be 6 cm. across. The wall contained crowds of Brenner nests, many showing pseudomucinous metaplasia, but one cyst only was much larger and comprised the main cyst which gave the tumour its macroscopic appearance. This showed as its lining a surface layer of mucin-bearing cells and beneath this a thick layer of typical Brenner cells many of which were vacuolated (Fig. 5). Unfortunately both the above tumours were observed before Teoh's paper of 1953 became available and no fat stains were done on fresh material to determine the nature of the stroma in either.

It would appear to be a matter of definition whether or not the last-described tumour is called a pseudomucinous cystadenoma. In many parts of the lining of the main cyst the underlying Brenner cells were missing and using ordinary stains these areas, if examined alone, would undoubtedly have been diagnosed as pseudomucinous cystadenoma. There seems no doubt, therefore, that such tumours can be produced by "metaplasia" from Brenner tumours, but this is not to say that all are. Further study of the stroma by histochemical methods would appear to be necessary for Brenner tumours and pseudomucinous cystadenomas.

There seems little point in repeating yet again the classical arguments on this subject. It is evidently very rare to observe Brenner cells beneath the lining of pseudomucinous cysts. On the other hand, one could well imagine that, were the Brenner cells to be squeezed out, or otherwise removed, the tumour which is the main subject of this paper would present the typical appearance of a multiloculate pseudomucinous cystadenoma. It is hard to imagine how such a removal could take place or that it could do so with remarkable completeness so remarkably often.

(b) *Relationship to Walthard Cell Nests*

In this series Walthard cell nests were observed only in Mrs. M.'s tumour. This is not to say, of course, that they were certainly not present in the others. Moreover, in her case they were found only in one block and that after several copies had been cut from it for different purposes. Teoh's histochemical studies appear to prove that the resemblance between their cells and those of Brenner tumours is fortuitous, but I feel that the resemblance is closer than he admits, i.e., I am sure that mucin-bearing acini are present sometimes in the cell nests. I have not observed this outside Mrs. M.'s tumour and it may be that both types of cell are responding to some outside stimulus to produce mucin in relatively large amounts. The present cases do not, indeed, shed any light on the problem.

(c) *Significance of Hormonal Activity*

In all the cases of this series tube, endometrium or both were available for histology and none showed any hyperactivity with the exception of Mrs. M.'s. Five were discovered in postmenopausal women and only one of these experienced vaginal bleeding. No cause for this symptom was found. In these days of frequent

hormonal medication it is, of course, extremely difficult to be certain that a patient is not receiving oestrogens. She may deliberately deceive or be unaware of what she is taking. The trouble is familiar to every practising clinical gynaecologist, but a pathologist may be permitted to record that he has seen two women with post-menopausal bleeding and hypertrophied endometrium who denied all medication. One was found by the Ward Sister to be taking oestrogen tablets deliberately, while in the other it was discovered that she was receiving oestrogen cream to apply to a radium scar on her face. When this was discontinued her complaint ceased. It is evident that in some women the endometrium remains much more sensitive to oestrogens after the menopause than in others.

There are, however, a number of cases recorded in the literature of post-menopausal bleeding with endometrial hypertrophy associated with the presence of a Brenner tumour. Marwil and Beaver (1942) is a recent and readily-available reference. Mrs. M. may well be an authentic case. If so, the striking thing about her tumour was the relatively enormous mass of Brenner cells involved when the papilliferous cyst linings are considered, far more than are found in the usual small, fibrous tumours of the type, even when the cell nests are crowded together. It must be emphasized that the cells were certainly not of the granulosa type and that no large collections of granulosa cells were found, although plenty could have been hidden away in the areas not examined. These Brenner cells were markedly specialized histologically but this does not mean that they were necessarily specialized functionally. If Teoh's idea that both Brenner and granulosa cells are of follicular origin is true, it may be that Brenner cells retain the power to produce oestrogens to a very small degree and that large numbers may be required to produce much effect, while a particularly sensitive endometrium may be needed.

Summary and Conclusions

A detailed account is given of an extremely florid Brenner tumour showing papilliferous cysts lined by the characteristic cells and with marked pseudomucinous metaplasia. Walthard cell nests were present also and post-menopausal hypertrophy of endometrium and of tubal mucosa. The tumour is compared with seven other Brenner tumours.

One other of these showed pseudomucinous metaplasia of sufficient degree to produce what could only be described as a pseudomucinous cystadenoma, but this does not imply that the appearance is a common one.

Brenner and Walthard cells can both undergo pseudomucinous metaplasia, but once again this does not imply identity.

If Brenner cells are derived from follicular epithelium they may retain oestrogenic properties, but to a lesser extent than granulosa cells.

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MELAENA NEONATORUM

BY

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MELAENA is an alarming and often a serious symptom. Although its frequency in the first week of life may be diminishing it was always an uncommon event and even early accounts (Townsend, 1894; Javert, 1938; Salomonsen, 1939) suggest an incidence of 7 or less for every 1,000 births. But if infrequent it can still be dangerous and, of 58 infants admitted with melaena neonatorum to the Children's Department of the teaching hospital in the past eight years, 5 died. For a quarter of a century investigation, management and prevention have centred mainly on the relationship between apparently spontaneous haemorrhage at this age and the temporary deficiency of prothrombin and other factors concerned with blood coagulation. We have nothing to add to this important aspect but our experience in this hospital from 1948 to 1955 suggests that there are essentially two distinct and unrelated processes which can lead to melaena in the first 4 days of life. Shaw (1913) emphasized in the *Doctor's Dilemma* that most important medical observations need to be remade at regular intervals. It is the purpose of this paper to draw attention again to a common but forgotten process in the production of neonatal melaena.

It was in 1948 that our conventional thinking about melaena in the newborn was questioned by the following experience. A woman of 19 was admitted in the 38th week of pregnancy. The onset of labour was complicated by a non-toxic accidental haemorrhage. The time of rupture of the membranes is uncertain, but at least a pint of blood was lost in the first hour of labour and then bleeding gradually ceased until delivery 9 hours later. The infant weighed 7 pounds and was normal at birth except for the astonishing amount of blood which poured from the nose and mouth. Melaena first appeared 17 hours later and during the next 16 hours 5 more tarry or dark blood-containing stools were passed. Throughout his stay in hospital the infant remained well and his haemoglobin did not fall. The only satisfying explanation at the time was that the melaena had arisen, not from spontaneous intestinal haemorrhage, but from maternal blood swallowed during birth. After this experience we attempted to decide to which of these categories each melaena properly belonged. Attempts to show that the blood came from the mother by establishing "group" differences between the infant's red cells and the stool failed because the stool red cells were invariably haemolyzed. In the past year, however, by the use of a test which differentiates foetal from adult haemoglobin (Singer, Chernoff and Singer, 1951), we have established the existence of melaena from swallowed maternal blood in 3 infants and justified the belief in its existence which had been held in the hospital since 1948.

THE CLINICAL PICTURE OF MELAENA NEONATORUM FROM 1948–1955

A review of melaena in the hospital over the past 8 years suggests that in almost every case the difference between spontaneous bleeding and swallowed blood can be determined on clinical grounds. During this period there were 37 infants with sufficient blood in their stools to justify the term melaena. (We stress quantity in our definition because from time to time we see flecks of bright blood mixed with mucus in the early days of life; these have not been included in the group under consideration.) After careful consideration of the pregnancy, the labour, the character of the stools, and the behaviour of the

infant in the first week of life, we divided the 37 into two main groups; 17 with apparently spontaneous bleeding from the bowel, and 18 in which it certainly or very probably arose from swallowed maternal blood during birth. In the remaining 2 the precise origin of the blood was not decided. We have called the two groups "endogenous" and "exogenous" melaena.

Endogenous Melaena

Although no special haematological studies were made, the timing, duration, and isolated character of the episode led us to the conclusion that the 17 infants were a uniform group and probably had haemorrhagic disease of the newborn. Thirteen of the infants were mature and 4 were premature. From Table I it is clear that melaena occurred later than in the infants who were thought to have swallowed blood. In 14 it occurred between 24 and 60 hours after birth, in 2 at 76 hours and in only 1 infant on the first day of life. The average number of blood-containing stools was 4 with a range from 1 to 6 and the average duration of the melaena 19 hours with a range from 4 to 36 hours.

The potential seriousness of endogenous melaena is shown by the fact that 5 of the 17 infants needed blood transfusion. In 2 infants 40 ml. and 65 ml. of fresh blood were given to arrest bleeding, but in the remaining three, 100 ml., 130 ml. and 250 ml. were required to deal with the rapid blood-loss. In the last child it is certain that, if the transfusion had not been started immediately the first large melaena appeared, the child would have died. Two further facts emphasize the continuing danger from endogenous bleeding. In our general hospital experience during the eight years under review, 58 newborn infants were admitted with melaena and 5 died, and the total deaths from this cause in England and Wales for the eight year period from 1947 to 1954 were 1,721.

Exogenous Melaena

In this group, the first appearance of melaena was much earlier, being on the first day of life in all, in 14 within 12 hours, and in 6 within an hour of birth. The average number of blood-containing stools was 8 or twice as many as in the infants with spontaneous bleeding and with a range from 4 to 17. This is very similar to Apt and Downey's (1955) experience in Boston where in 7 infants with melaena from swallowed blood the average number of abnormal stools was 9 and the range, as in our series, from 4 to 17. The melaena in our experience also lasted longer with an average duration of 40 hours and a range from 21 to 64 hours. It is clear that exogenous melaena tends to be more intense and to last longer than the endogenous variety. Half the affected infants were premature. With one exception the infants remained in excellent condition throughout and there was no clinical anaemia. We cannot be certain on this last point because although the haemoglobin was estimated in 10 infants during or after the melaena and found to be normal, in only 4 was the number and timing of the estimations sufficient for proof.

Table II shows clearly that over the whole

Table I

The Time When Melaena First Appeared in 35 Infants

Time (hours)	–1	–6	–12	–18	–24	–36	–48	–60	–72	–84
Endogenous	–	1	–	–	–	7	4	3	–	2
Exogenous	6	3	5	1	3	–	–	–	–	–

Table II

The Yearly Incidence of Melaena in this Hospital from 1948–1955

Year	1948	1949	1950	1951	1952	1953	1954	1955
Endogenous	5	2	3	3	2	2	0	0
Exogenous	1	2	4	1	1	1	4	4

period, melaena from swallowed maternal blood was as common as melaena from spontaneous intestinal bleeding and in the past 2 years it has been the only variety met with in the hospital. The numbers in each year are too small to claim a true decline in endogenous melaena though we suspect that such is the case. Vitamin K is not given to the mothers during labour, but since 1949 all premature infants and all infants experiencing an instrumental or other difficult form of delivery have been given vitamin K, 10 milligrams in watery solution, within 5 minutes of birth or as soon as the infant's airway was clear. In the past year smaller doses of the vitamin have been used especially in premature infants.

The Circumstances Preceding Exogenous Melaena

The 18 pregnancies were all complicated by ante-partum haemorrhage. There was, however, no uniform pattern of maternal bleeding; in 11 it was due to non-toxic accidental haemorrhage, 4 had placenta praevia, in 2 the bleeding was associated with toxaemia and in the last mother the labour was thought to be normal until the membranes ruptured just before delivery and the liquor was found to contain clots of blood. There was no velamentous insertion of this last infant's cord and he did not become anaemic. The maternal bleeding began at different stages in pregnancy from the 29th week until term. In 10 women the bleeding continued throughout labour and in a further 5 it was present at the beginning or during the early stages of labour. The delivery of these 5 infants occurred 5, 9, 10, 27 and 33 hours after the cessation of bleeding. In the remaining 3 infants there was an interval between the apparent end of the maternal bleeding and delivery of 31 hours and 4 and 5 days. In spite of this delay large amounts of clotted blood were removed from the mouth and pharynx of the last 2 infants at birth. A careful review of the duration of bleeding, the time when the membranes ruptured and the length and character of the labour do not explain where and when the blood is actually swallowed. Apt and Downey's (1955) 7 cases of exogenous melaena all occurred in women with placenta praevia; they stated that in 5 the amniotic fluid was "bloody" and 4 of the infants were delivered by Caesarean section. They suggested that "on occasion when a marginal separation of the placenta takes place, rupture of the chorion laeve and amnion in the adjacent area may also occur. The chorionic plate in the region of the marginal sinuses containing maternal blood is thin and this dissection of the blood through the thin amnion into the amniotic fluid is feasible." Although this may hold for some cases of placenta praevia it does not explain where and when the blood was swallowed in the majority of our patients who had accidental haemorrhage.

That the actual swallowing of blood can occur quite quickly in the vagina is illustrated by the following experience. A twin pregnancy was interrupted at the 38th week by a toxic accidental haemorrhage. Because of foetal distress the first twin was delivered by forceps 9 hours after the onset of bleeding. Six minutes later the second twin was delivered by internal version and breech extraction. The liquor in the second sac was quite clear but a considerable quantity of blood was present in the vagina. The first twin was unaffected but at 17 hours the second started a heavy melaena. His general condition and haemoglobin levels were excellent throughout the stay in hospital and there seems little doubt that the blood responsible for the melaena was swallowed during his passage through the vagina.

Another woman had a sudden accidental haemorrhage at the 30th week of pregnancy. No further bleeding occurred but, when the infant was born 4 days later, the mouth and pharynx were full of clots, and 35 minutes after birth melaena began. Ten blood-containing stools with adult haemoglobin were passed during the next 36 hours. As the exact time when the membranes ruptured is unknown the blood may have been swallowed *in utero*, or, in common with the second twin described above, swallowed from residual blood remaining in the vagina from the haemorrhage 4 days before.

A third woman was well until she went into labour at term. The membranes ruptured 4 hours before delivery and the labour lasted four and a half hours. With each contraction there was slight bleeding from a type 1 placenta praevia.

Melaena first occurred at the actual moment of birth and during the next 36 hours the infant had one haematemesis and 4 tarry stools. His condition was excellent throughout his stay and the haemoglobin levels at 49 hours and on the 6th day were 14·7 and 15·4 g. This case is similar to those described by Apt and presumably the blood was swallowed *in utero*.

In our 4th example the labour which lasted 11 hours was considered completely normal until the membranes ruptured 20 minutes before the birth of the child. The liquor contained meconium and clots of bright red blood. Melaena started 45 minutes after birth and 7 blood-containing stools were passed in the next 44 hours. No anaemia developed and the infant's condition remained excellent throughout his stay.

The Mechanism of Exogenous Melaena

It is evident from the four examples that in many cases the place and time when the blood is swallowed remains uncertain. It is equally clear that clinical observation alone does not tell us how much blood an infant needs to swallow before melaena occurs. When we first considered this problem in 1948 we found no existing answer and there was considerable doubt amongst our obstetric colleagues whether an infant could swallow sufficient blood to produce the striking melaena we had seen.

The question has recently been investigated by Apt (1955) and his findings are given in modified form in Table III. Apt gave varying amounts of blood to two groups of newborn infants. First a group of 41 who were only a few hours old. Using an intragastric polythene tube from 15 to 40 ml. were given and no other fluids allowed for the next 24 to 36 hours. The second group were between 3 and 4 days old and had all passed meconium. Provided that at least two previous stools were free from occult blood 10 to 40 ml. of cord or adult blood were given by the same method and then normal feeding was resumed. It will be seen from Table III that, for infants receiving blood within a few hours of birth, from 35–40 ml. was necessary to produce bloody stools in the majority. Melaena began as early as 9 hours or as late as 30 hours after intragastric administration and continued over periods varying from 12 to 45 hours. On the third and fourth day of life when meconium had been passed, as little as 10 ml. was capable of producing bloody stools. These appeared from 3 to 10 hours after instillation and melaena continued for a further 1 to 14 hours. It would seem that, although as little as 10 ml. can produce 1 or 2 dark stools, between 1 and 2 ounces

Table III

The Effect of the Intragastric Administration of Blood on the Stools of Newborn Infants (Apt, 1955)

Amount of Blood (ml.)	No. of Infants Receiving Blood	Grossly Bloody Stools			
		No. of Infants	First Noted Range in Hours	Duration Range in Hours	No. of Stools
A. During Meconium Period					
15	8	2	19–30	14–	1–3
20	7	2	17–18	32–40	4–6
25	3	2	15–18	–40	1–6
30	15	8	9–30	12–45	2–7
35	5	4	9–15	20–37	4–9
40	3	3	10–20	14–28	4–7
B. After Meconium Period					
10	10	10	3·5–10	1– 9	2–3
15	5	5	2·5–10	1·5–14	1–4
20	5	5	3–12	3–15	2–5

of blood must be swallowed for the striking melaenas seen in the first days of life.

Additional Observations

Although we have emphasized the importance of melaena from swallowed maternal blood, 4 of the 18 infants also had a single haematemesis. In the 17 infants with true haemorrhagic disease there were 7 with haematemesis. Also in a proven exogenous case the infant had haemoptysis from inhaled maternal blood as well as haematemesis and melaena. At the 30th week of her pregnancy and 14 hours before delivery this infant's mother bled suddenly from a non-toxic accidental haemorrhage. At birth bright blood poured from his mouth and nose and was almost immediately followed by melaena, which recurred several times before the child's death at 4 hours. Autopsy revealed maternal blood in both the intestine and the lungs. This experience shows that quite apart from the anoxic threat to the foetus in ante-partum haemorrhage, inhalation of maternal blood in the course of labour may on occasion prove fatal.

Summary and Conclusions

Melaena from swallowed maternal blood during birth is now the commonest cause of melaena neonatorum in this hospital. This exogenous form has been as frequent over the past 8 years as endogenous bleeding from true haemorrhagic disease of the newborn.

The condition was well known to the German obstetricians in the early years of this century (Kamann, 1907), and we regret our earlier ignorance of their straightforward observations.

The introduction of a simple and reliable test for foetal and adult haemoglobin in stools has now made it possible to differentiate endogenous and exogenous bleeding in almost every case where it can be promptly applied. The following clinical features would also suggest that a melaena was arising from swallowed blood.

(1) The association with a pregnancy complicated by ante-partum haemorrhage and with the bleeding continuing up to and in many cases for part or all of the labour.

(2) The melaena starts invariably on the first day of life and generally within the first 12 hours.

(3) The abnormal stools will tend to be more numerous than in endogenous bleeding and will continue for periods from 4 hours to 3 days.

(4) Unless anoxia or other complications are present the child remains well throughout the experience and no anaemia develops. Yet since spontaneous or endogenous bleeding is always potentially dangerous serial haemoglobin estimations are still desirable in melaena neonatorum.

Though in Apt's experience as little as 10 ml. of blood could produce exogenous melaena in the natural condition infants probably swallow between 1 and 2 ounces. Although in placenta praevia blood may enter the amniotic cavity at the time of the premature placental separation and be swallowed by the infant *in utero*, it is also possible for blood to be swallowed in the vagina. In many cases, however, it is not clear when and where this event takes place. The recognition that melaena is arising from swallowed blood and not from spontaneous bleeding is important for the rational care of the child and the peace of mind of the obstetrician or paediatrician concerned.

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THE RESULTS OF SURGICAL INDUCTION OF LABOUR

BY

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SINCE Gibson (1952) made his valuable survey of Surgical Induction in Belfast, there have been two British publications assessing the results of induction, by Evans (1954) and Tennent and Black (1954) which reveal many discrepancies with reference to the hazards involved. The present report represents a further attempt to assess the results of surgical induction with particular reference, first, to the dangers inherent in the procedure for mother and child; and secondly, to the efficacy of the method chosen.

At the Birmingham Maternity Hospital, in the 3 years 1950–1952 there were 5,544 deliveries, and in 1,099 cases (19·8 per cent) labour was surgically induced. The records of these 1,099 cases form the basis of this report.

INDICATIONS

The principal indications for induction in the cases presented are listed in the table below.

TABLE I
Principal Indications for Surgical Induction

		Per cent
Hypertension and pre-eclampsia ..	452	41
Postmaturity	212	19
Disproportion (previous difficult forceps, etc.)	124	11
Breech presentation	70	6
Hydramnios	62	6
Unstable presentation	45	4
Intra-uterine death, ante-partum haemorrhage, diabetes, rhesus disease, and various other indications, including "doubtful"	134	13

These figures must be interpreted liberally, for in many cases a combination of indications was present and it was often difficult to decide in retrospect upon the chief of these. It is proper to comment that the large number of indications under the heading "postmaturity" reflects a belief widely held for some years in this hospital that there is a real risk to the foetus from undue prolongation of pregnancy and that surgical induction itself is, to say the least, a lesser evil in such cases. Nevertheless, there is no policy of inducing all cases at 41-weeks gestation, as described by Tennent and Black (1954), and each case is treated on its merits. An explanation of the policy of induction in breech presentation (which is not invariable in the hospital) is found in *Obstetrics and Gynaecology* by B. M. Willmott Dobbie.

METHOD

For the purpose of this investigation, surgical induction is held to mean artificial rupture of the amniotic sac (hindwaters or forewaters). Digital stretching of the cervix without membrane puncture is excluded, as is the use of laminaria tents, whilst bougies, stomach tubes and "bags" are never used in this hospital. Repeat inductions are likewise excluded.

The normal procedure at the time covered by this report involved exploring the cervical canal with the finger and sweeping the membranes from the internal os, followed by the passage of a Drew Smythe catheter, with release of liquor amnii from the hindwater sac. On occasion the forewaters were unintentionally ruptured during this procedure. An anaesthetic was not commonly given. When the os was quite unripe, the attempt was often abandoned, but sometimes the forewaters would be ruptured with an artery forceps. After puncture of the membranes, no further uterine stimulant was generally given for 24 hours, but thereafter a medical induction might be ordered if considered necessary by the consultant-in-charge.

(Since 1952, the intravenous pitocin drip has been used more frequently and forewater rupture has been more commonly performed, but it is the results of the older technique just described, which are to be studied now.)

Maternal Results

Maternal Mortality

There were 4 deaths in the 1,099 patients surgically induced.

Case 1. A primigravida, aged 36, was gravely ill with severe aortic incompetence. When 3 weeks overdue, she was induced because of a deterioration in her general condition. Considerable relief followed the release of much liquor, but she developed cardiac failure in labour and died soon after delivery.

Case 2. A gravida-5, aged 40, was admitted at 41-weeks gestation for induction of labour because of an unstable lie. After admission she had injections of 2 and 5 units of pitocin intramuscularly without effect. Surgical induction by Drew Smythe catheter was then performed. She went into labour 36 hours later and was delivered normally of a live baby. Despite the aid of ergometrine given on completion of the third stage, the uterus persistently relaxed, blood loss mounted and collapse occurred 1½ hours after delivery. Transfusion of 5 pints of blood failed to control the loss and death occurred 5 hours after delivery. Autopsy revealed no pathological source of bleeding.

Comment. In retrospect, this death could possibly be due to afibrinogenaemia; yet it is generally agreed that puncture of the membranes as such is likely to prevent rather than to cause such a condition (by preventing the escape of liquor under tension into the circulation).

Case 3. A gravida-2, aged 36, was admitted as an emergency, with eclampsia at the 29th week of her pregnancy. Twenty-four hours after admission labour was induced surgically by rupturing the forewaters. Labour did not commence and 4 days later her condition remained serious; the cervix was then stretched digitally. Six hours after this she developed contractions and delivered herself of a small male child. The toxaemia then cleared rapidly. Fourteen days after delivery she had a pulmonary embolus, and within an hour had a second, from which she died. There were no warning signs in the legs, and the only rise in temperature occurred on the night preceding her death (temperature 99·8°).

At post-mortem examination the leg veins contained no clot and the blood clot in the pulmonary artery appeared to have come from the internal iliac vein. A septic endometritis was present and many of the uterine veins contained infected thrombus.

Case 4. A primigravida, aged 30, was admitted at the 39th week of her pregnancy because of moderately severe pre-eclampsia. Surgical induction was performed on admission and the following day intramuscular pitocin was given and labour commenced.

A contraction ring dystocia developed and after a prolonged labour delivery was achieved by manual rotation and the application of forceps.

On the second day after delivery a temperature of 102° was recorded, but the pyrexia partially subsided on antibiotic therapy. Evening temperatures of 99° were noted, but on the fifth day the temperature rose again to 101·4° and the patient complained of chest pain of sudden onset.

Pulmonary embolism from a calf thrombosis was diagnosed and treatment with heparin commenced. Bilateral leg thrombosis recurred twice and bouts of pyrexia also recurred, despite energetic treatment with anticoagulants and antibiotics, and on the fortieth day after delivery a massive pulmonary embolus proved fatal.

The post-mortem examination showed the clot to have come from the femoral vein.

Comment. It appears that the induction cannot be inculpated in Cases 1 and 2, but may have been an aetiological factor in the deaths of Cases 3 and 4, through the introduction of infection.

Maternal Morbidity

Surgical induction might be justly criticized as causing harm to the mother (apart from trauma) in one of four ways—by introducing sepsis, by inducing an abnormal type of uterine action with its resultant difficulties, by exposing her to an increased chance of undergoing Caesarean section, and by causing anxiety and distress.

Although it is possible to cause direct traumatic damage with the Drew Smythe catheter, no such case appears in this series, but accidental haemorrhage following induction is mentioned later under complications of the procedure.

Sepsis

This was described by Peel (1936) as "first and foremost" of the maternal risks; but he referred to cases induced largely by bougie, and this method is now condemned, because of the risk of sepsis, by Gibson (1952) who finds the alternative artificial rupture of the membranes to be complicated by infection infrequently.

One hundred and fifty-one cases of notifiable genital pyrexia (2·7 per cent of all deliveries) were recorded in the hospital during the 3 years under review. Excluding emergency admissions it is found that in 3,811 deliveries in booked patients, there were 89 cases of notifiable (genital) pyrexia (2·3 per cent). In the 718 booked cases surgically induced there were 15 cases (2·1 per cent) and 6 of these 15 patients had operative deliveries and therefore a second potential source of infection. Gibson (1952) had a comparable figure of 4·1 per cent in his series, but this was inflated by his bougie inductions. Of the 883 cases in this series, who had a spontaneous delivery following induction, only 12 (1·4 per cent) ran a notifiable (genital) pyrexia in the puerperium. Certainly at this hospital it appears that the incidence of sepsis is not at present great provided that no further interference is required.

Abnormal Uterine Action

Various opinions have been expressed in the past on the *quality* of labour which follows surgical induction.

Eastman (1938) believed the average length of labour to be shortened by nearly 50 per cent. Tennent (1938) stated it was unaffected, whilst Peel (1936) said "quite often the uterine action in labour is inadequate so that such complications as inertia, contraction rings . . . are more common".

Amongst the 1,099 women under review, there were only 11 cases in whom labour lasted more than 48 hours comprising 9 hypotonic inertias and 2 disordered uterine actions. In a further 13 cases, however, failure to progress in labour led to the performance of Caesarean section in less than 48 hours. Furthermore, in another 20 cases, failure to progress in labour was added to some other primary indication such as deteriorating pre-eclampsia, in coming to a decision to operate.

It appears then that among 1,063 women who went into labour following induction, there were at least 15 cases of hypotonic inertia and 9 cases of disordered action severe enough to cause prolongation of labour beyond 48 hours or to lead to Caesarean section. Whether this constitutes a definite increase in the dystocia rate for such a selected group of women is more difficult to say. It is worthy of note that 4 of the 9 cases of disordered action also had intramuscular oxytocin.

Caesarean Section

This is perhaps the most difficult part of the report upon which to give an unbiassed opinion. Eighty-two cases had Caesarean section following surgical induction (7·4 per cent). (The overall rate of delivery by Caesarean section for the hospital during the same time was 14 per cent.) In 36 cases, the operation was done before the onset of labour. In many cases, e.g., severe pre-eclampsia or postmaturity confirmed at membrane puncture, Caesarean section was undertaken if labour had not commenced within a short time after the induction: and in such cases a more radical opinion would have advocated omission of the preliminary step. But it is felt here that a number of such women will deliver quickly after membrane puncture and thereby be spared abdominal delivery; such a procedure is given the name "trial of puncture" or "trial induction".

The indication for performing Caesarean section was generally the indication for the induction plus one or more of the following factors:

(*a*) Failure to go into labour (32 cases)
(*b*) Failure to progress in labour (33 cases)
(*c*) Foetal distress (8 cases)
(*d*) Prolapse (or presentation) of the cord (5 cases)
(*e*) Occurrence or recurrence of malpresentation (4 cases).

The induction itself must be held responsible for the Caesarean section in a total of at least 9 cases under sections (*d*) and (*e*). To this number, critics of the policy of induction might reasonably add several cases of disordered action and some (but not all) of the cases induced for disproportion. Nevertheless, it is important to observe that, in the long view, some cases must surely have been *saved* from Caesarean section by timely surgical induction. In such a study as this we see the debit-side of the balance sheet clearly, but the credit-side only hazily and our idea of the true state of affairs must therefore remain a little obscure.

It may justly be argued that surgical induction should be avoided where subsequent Caesarean section seems likely, because of the risk of sepsis. Indeed, in Gibson's (1952) series, 6 of the 34 patients who had a Caesarean section developed a notifiable pyrexia and 2 patients died. Among our patients, 8 of the 82 ran a notifiable pyrexia and, though no patient died, it will be agreed that the pyrexia rate in both series is high.

It is in this section, perhaps, and under the headling of sepsis that the main criticisms of a *policy* of induction will lie.

Psychological Upset

The patient who realizes that she has had an induction is subject to anxiety until her delivery is accomplished. She justly assumes that all is not well and anxiously awaits the onset of her pains. The retraction pains which take up the loss of volume consequent upon puncture may often be thought to indicate the onset of labour and disappointment when they subside may be acute. Sleep may be lost and if oxytocics add further painful insult to the uterus without initiating effective contractions, the patient may be far from well when labour does finally commence. It is an important task for her attendants to keep her in good heart during this time; and it is important to avoid unnecessary inductions, if on these grounds alone.

A worthwhile subterfuge in some cases is to refer to the procedure as primarily a "test of the waters" which sometimes brings on early labour —relegating the induction to a secondary place in the patient's mind.

Foetal Results

In assessing the results of surgical induction in relation to the child, one controversial issue overshadows the rest, viz., the value to the baby of an intact amniotic sac in labour. The destruction of the foetal bath of liquor amnii must result in the loss of hydraulic "cushioning" during contractions. After membrane puncture it might be contended that a material limitation of the foetal blood flow through the placenta should result. Evans (1954) suggests that this is so, and Gibson (1952) believes that the risk is appreciable after 72 hours. If it were true, then surgical induction of labour would have to be made responsible, in part at least, for all deaths (following its use) from intra-uterine asphyxia and placental insufficiency even when severe pre-eclampsia, hypertension or postmaturity appear to be the primary factors. In postmaturity the results after induction might be expected to be worse or no better than when a policy of expectancy is pursued. Yet the reports of Racker, Burgess and Manly (1953) and of Tennent and Black (1954) do not suggest it. Since the question is not finally resolved, in the breakdown of mortality figures in this section of the report I have included only those cases where the induction seems indisputably responsible for foetal death.

Foetal Mortality

The total foetal loss (stillbirths and neonatal deaths in hospital combined) was 100 (9·1 per cent), of which 73 were stillbirths and 27 neonatal deaths. Of the 73 stillbirths, 13 were induced because of a known intra-uterine death. The chief cause of death in the remaining 60 was as follows:

Congenital abnormalities	27
Accidental haemorrhage (6 before and 4 after induction)	10
Pre-eclampsia and hypertension (prematurity)	10
Postmaturity	3
Prolapsed cord	3
Posterior placenta praevia	2
Intra-uterine infection	2
Intra-uterine asphyxia (severe cardiac disease)	1

Breech delivery (cerebral haemorrhage) ..	1
Erythroblastosis	1

The induction must be held responsible for 4 stillbirths the result of placental separation, for 3 from prolapsed cord, and for 2 from intrauterine infection. It is admitted, as previously mentioned, that it might have been a factor, but not the only one in the death of some other babies.

Of the 27 neonatal deaths induction did not appear to be responsible for the death of the child in 24 cases. The cause of death in these cases was as follows:

Prematurity (pre-eclampsia)	7
Congenital abnormalities	6
Erythroblastosis	4
Cerebral haemorrhage (breech: forceps) ..	2
Atelectasis (prolonged labour)	1
Maternal diabetes	1
Hyaline membrane	1
Unexplained	2

In 3 cases death was attributed to the induction. One baby died from an infection probably acquired *in utero* and another from prematurity due to induction being performed at the 35th week instead of the 39th as was at first believed. The third case was an unstable presentation induced after correction of a transverse lie. The malpresentation recurred and the baby's shoulder became impacted in the pelvic brim.

Thus, in 1,099 inductions responsibility must certainly be accepted for the death of 12 babies (1·1 per cent); from placental separation 4 cases, prolapse of the cord 3 cases, intrauterine infection 3 cases, 1 error in the maturity estimation and 1 impacted shoulder presentation. (The comparable figure from the same causes in Evans's series was 2·02 per cent.)

Foetal Morbidity

It was expected that a close scrutiny of the more severe neonatal infections would show a number due to infection acquired *in utero* as a result of puncture of the membranes. This, however, did not prove to be the case, although several babies suspected of having acquired such an infection were treated at once with antibacterial agents. A careful search into the separate records kept by the paediatricians has confirmed this somewhat unexpected observation.

EFFICIENCY OF SURGICAL INDUCTION

Of 1,099 women surgically induced, 36 were delivered by Caesarean section before the onset of labour and a further 46 after the onset of labour.

Of the 1,063 women who commenced labour after induction, it has been possible to plot the interval between induction and the onset of labour (the I.L.I.) against the duration of pregnancy in 1,005 cases. Of the 1,017 who completed a vaginal delivery after induction it has been possible to graph the induction to delivery interval (the I.D.I.) against gestation in 967 cases. The number discarded because of deficiencies in the records is therefore approximately 5 per cent in each group.

Figs. 1 and 2 give the results of this study in tabular form for primigravidae and parous woman respectively.

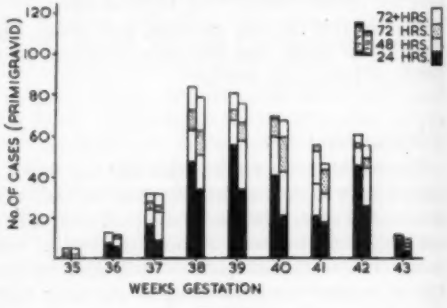

FIG. 1

Comparison of the interval between induction and the onset of labour (I.L.I.) and the interval between induction and delivery (I.D.I.) at different periods of gestation in primigravidae.

Although the Induction to Delivery Period can be more accurately determined it is the latent period from induction to the onset of labour which interests us most. A comparison of the two intervals (I.D.I. and I.L.I.) shows no apparent discrepancy if allowance is made for the slightly longer duration of labour in the average primigravida. The I.L.I. is therefore used subsequently for discussion purposes.

The number of patients in labour within

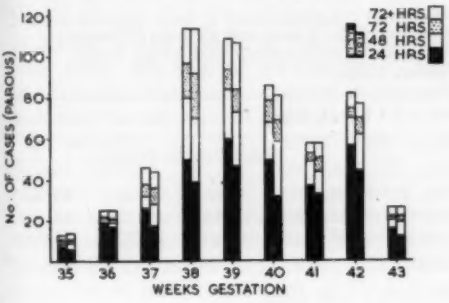

FIG. 2

Comparison of the interval between induction and the onset of labour (I.L.I.) and the interval between induction and delivery (I.D.I.) at different periods of gestation in parous women.

24 hours of induction represented 60 per cent of the total (604 out of 1,005) and within 48 hours, 80 per cent (801/1,005). This average is notably less than that quoted by Gibson (1952), Lemmon (1948), and Tennent and Black (1954). Gibson (1952) points out that rupture of the hindwaters is less effective in this respect than a forewater puncture and this fact may account for the difference. If in addition the Birmingham figures are "weighted" by a group or groups of cases which are ill-suited for induction, this will become apparent on further breaking down the results of induction for different indications. (In fact, no such group was found.)

Parity

The I.L.I. for primigravidae and multigravidae at different gestations is summarized in Table II. The primigravidae include a relatively large number of toxaemic patients (50 per cent compared with 29 per cent in the multigravidae) and this makes comparison between the results in the two categories of patients unreliable, especially in the earlier weeks. However, a comparison of the columns for term (40 and 41 weeks) and beyond (42 weeks plus) in which there is much less toxaemia shows that the multipara is certainly no more liable to go into labour than the primigravida following induction. Gibson (1952) points out that parity has no influence on the ripeness of the cervix.

Maturity

It is generally accepted that the success of an induction is dependent upon the ripeness of the cervix, and it is self-evident that the cervix will more commonly be ripe at term than in the earlier weeks. In this series, where induction is frequently carried out before the cervix would satisfy the usual criteria for ripeness, there is, surprisingly, no apparent difference in the results of induction at term compared with the 35th to 37th weeks, and this is true for primigravidae and for parous women.

Evans (1954) makes the same comment, and there would seem to be an implication here that ripeness of the cervix is an all-or-none quality. Another explanation is that the inductions prior to term (done largely for pre-eclampsia) form an especially amenable group; this will be examined in the next paragraph.

RESULTS OF INDUCTION IN SPECIFIC CONDITIONS

Pre-eclampsia

This group includes many cases of pre-eclampsia complicating essential hypertension (i.e., cases in whom albuminuria or generalized oedema appeared) as well as "primary" pre-eclampsia.

The figures (see Table II) are based on 381 cases. (Thirteen cases had Caesarean section before the onset of labour and 15 cases had to be discarded.)

Comparison with the overall figures, which include the toxaemic, shows a very close similarity, but this may be misleading, especially in the early primigravidae, where there are almost no non-toxaemic patients for comparison.

The answer to the question "does pre-eclampsia itself predispose to easy induction?" was therefore sought in another way. The records of all cases of *severe* pre-eclampsia were examined carefully, the criterion of "severe" being an Esbach recording of 5 g. or more of albumin/litre.

One hundred and three such cases were treated in hospital from 1950–1952, 62 primigravidae and 41 parous women. In 13 cases (including 7 primigravidae), labour commenced spontaneously, 5 of them before the 36th week (2 of the 5 in association with an accidental

TABLE II

Numbers (with percentages in brackets) of women in labour within 24 hours and 48 hours following induction at different periods of gestation; comparing results in pre-eclampsia with overall results for primigravid and parous women

Induction to Labour Interval (I.L.I.) <24 hours

	All Patients				Pre-eclamptic Patients			
Gestation in weeks ..	35–37	38, 39	40, 41	42, 43	35–37	38, 39	40, 41	42, 43
Primigravid	26 (52)	104 (63)	78 (62)	55 (75)	21 (54)	56 (60)	32 (52)	10 (83)
Parous	53 (63)	110 (50)	87 (60)	73 (68)	20 (65)	44 (61)	28 (72)	5 (63)

Induction to Labour Interval (I.L.I.) <48 hours

	All Patients				Pre-eclamptic Patients			
Gestation in weeks ..	35–37	38, 39	40, 41	42, 43	35–37	38, 39	40, 41	42, 43
Primigravid	39 (78)	131 (79)	113 (90)	65 (89)	31 (79)	73 (78)	54 (87)	12 (100)
Parous	60 (71)	164 (74)	117 (81)	90 (83)	22 (71)	60 (83)	37 (95)	7 (88)

Total numbers: Primigravidae .. 428; Parous 577

Numbers of pre-eclamptic: Primigravidae .. 216; Parous 164

haemorrhage). Thirty-one women had a Caesarean section of election (21 were primigravidae, and 22 of the 31 less than 36 weeks pregnant). In the remaining 59 cases, surgical induction was performed. Eleven of the 59 had a Caesarean section because of failure to achieve delivery within a reasonable time (6 before and 5 after the onset of labour). The remaining 48 comprising 28 primigravidae and 20 parous women had a vaginal delivery. A chart demonstrating the relationship between the I.L.I. and period of gestation in the 53 cases who commenced labour has been prepared (see Fig. 3).

Induction was usually undertaken only if the cervix allowed the introduction of a finger—cases with a tight os being commonly delivered by Caesarean section—but certainly many cervices were far from "ripe" at induction. Reference to Fig. 3 shows that 27 of 31 primigravidae, including several cases in the 7th and 8th month, were in labour within 48 hours of the induction. The parous women, on the other hand, were sharply divided in their response. Twelve were in labour within 24 hours, while 9 of the remaining 10 were not in labour 3 days after the induction. This does not reflect a more ready recourse to Caesarean section in primigravidae for only 3 primigravidae had a

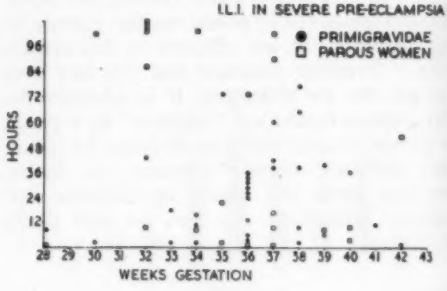

FIG. 3

Showing the interval between induction and the onset of labour at different periods of gestation for primigravidae and parous women with severe pre-eclampsia.

Caesarean section after induction and prior to the onset of labour. It does, however, show that, although the patient with pre-eclampsia may not always respond dramatically to induction, in this series an improvement in her general condition has often followed it, such as to allow somewhat prolonged delays.

To get an unbiassed picture, it must be noted that during these 3 years there were 4 cases of pre-eclampsia (3 of them severe, as defined here) who, after induction, developed eclamptic fits,

2 intra-partum and 2 post-partum. This must be debited to the method of treatment. On the other hand, one case of pre-eclampsia undergoing elective Caesarean section had an eclamptic fit during the induction of anaesthesia.

In summing up, there seems some weak clinical support for the view that the pre-eclamptic patient has an "irritable uterus" and may respond readily to induction. Our results do not compare, however, with those quoted recently by Townsend (1955) who, in a similar series, found that 97 per cent of his induced cases were in labour within 48 hours. Also, our incidence of Caesarean section (41 per cent) is notably higher than that quoted by Kellar (1955) (20 per cent) and Townsend (1955) (15 per cent) in this type of case.

Improved results should follow the advent of the "Pitocin drip" and it may safely be said that the results quoted here justify a trial induction in pre-eclampsia whenever the cervix will admit a finger.

Postmaturity

It was thought obvious that if induction should meet with particular success in any single group, it would be in patients induced under this heading; it was soon apparent that many of our patients did not fulfil the conditions required for the label of genuine postmaturity, but all were believed to be past term. No detailed analysis of the whole group has been undertaken, but certain facts have been established.

Two hundred and twenty-two cases were induced because of the risks of prolonged pregnancy, when they were considered to be overdue by a variable interval. Twenty cases were subsequently delivered by Caesarean section, 7 before labour had commenced (6 because of delay in starting in genuine cases of postmaturity, 1 from prolapse of the cord) and 13 after the onset of labour. In 5 of these 13 the reason was foetal distress, in 1 a compound presentation occurred, and in 6 there was undue delay in labour, 3 of them having a disordered uterine action. In 16 of these 20 cases, the induction was performed solely because of postmaturity, in the others disproportion and toxaemia were additional indications.

Of 215 cases who went into labour after induction, 145 were in labour within 24 hours (67 per cent) and 183 within 48 hours (85 per cent). Thirty-two were said to have an I.L.I. of over 48 hours. The records of these 32 cases were examined in detail. Only 16 of the 32 were found to be certainly 42-weeks pregnant or more at the time of induction and only 5 of the 16 showed confirmatory evidence of postmaturity (small amount of liquor and the typical appearance of the baby as described by Clifford (1954)).

Nevertheless, 5 cases showing clinically confirmed postmaturity failed to respond to surgical induction within 48 hours. Four were primigravidae and 1 was gravida-2. Two of these 5 babies were stillborn. A typical case history of one of these cases is given in brief:

> Mrs. B., a primigravida aged 35, with a regular monthly cycle, was admitted to hospital when she was 2 weeks overdue. Medical induction with castor oil, bath and enema failing, a surgical induction was performed using the Drew Smythe catheter. A small amount of clear liquor was obtained. Labour did not commence for 72 hours but then rapid progress was made. At three-quarters dilatation the foetal heart became irregular. The baby was delivered by low forceps, but the foetal heart had not been heard prior to delivery, and the baby was stillborn. The baby weighed 8 pounds 4 ounces, measured 22½ inches and the placenta had a "gritty" surface.

In another case labour did not commence for 3 days. When it did, foetal distress appeared and a rapid Caesarean section failed to save the baby. A third stillbirth occurred in early labour in a patient in whom there was no delay following induction. The only other baby lost in this group of patients was stillborn due to prolapse of the cord.

In conclusion, two points appear especially noteworthy. First, if we examine the small number of women who, after surgical induction at 42 weeks gestation are not established in labour within 48 hours (16 cases), we find in this group 2 stillbirths due to postmaturity. Secondly, if we look back to the small group of patients in whom Caesarean section following induction was performed chiefly because of a disordered action, 3 of the 7 patients thus classified had prolonged pregnancies. Thus, amongst women induced when overdue by 2 weeks or more, there is a troublesome minority (mainly primigravidae) who will not start in labour or who develop a disordered action; they may

require a Caesarean section to avoid a stillbirth. In cases of genuine postmaturity (confirmed at membrane puncture) delivery should be completed, if necessary by Caesarean section, within 48 hours of induction.

Complications of Surgical Induction

Prolapsed Cord

There were 11 cases of cord prolapse (1·0 per cent) and, as in all other series, it tended to occur in association with an unstable lie, malpresentation, hydramnios or a high presenting part. (Two cases of cord *presentation* in patients who were induced are included in the 11 cases of prolapse.) In such women it is obvious that spontaneous rupture of the membranes might equally bring about a prolapse of the cord; but the accident might not occur then until late in labour when vaginal delivery of a live baby could more frequently be achieved. To determine the truth of this, the records of prolapse of the cord occurring in booked patients in the hospital were studied.

During the 3-year period there were 3,811 deliveries in booked patients. Of this number 718 were surgically induced and 9 of these women (1·3 per cent) experienced prolapse of the cord; 5 of the 9 women had a Caesarean section and 2 babies were stillborn.

Amongst the 3,093 booked patients not surgically induced, there were 26 cases of prolapsed cord (0·8 per cent), 8 babies being lost and 8 being treated by Caesarean section. (In all cases the actual prolapse occurred after the patient's admission to hospital.)

These figures suggest that cord prolapse will not be much less common where surgical induction is done infrequently, though a more conservative attitude might reduce the number of Caesarean sections without a corresponding increase in the foetal loss. Gibson (1952) had only 1 case of prolapsed cord in 731 artificial ruptures of the membranes and Tennent and Black (1954) 1 case only in 1,585. These latter figures are notably different from those of Evans (1954) who had 16 cases in 507 membrane punctures (3·7 per cent) and the present series strikes a balance between these two extremes.

Accidental Haemorrhage

There were 4 foetal deaths from this cause following induction, 2 of which occurred in association with gross hydramnios. In the other 2 cases, there was reason from the case-notes to suspect some excess of liquor amnii. Further, it was noted that amongst 81 women with hydramnios who were surgically induced there were 5 cases of ante-partum haemorrhage due to the induction.

There seems good reason to think that hydramnios would generally be better treated by trans-abdominal paracentesis uteri, and if surgical induction is avoided in such cases, the risk of placental separation due to the procedure seems small.

Malpresentation

When malpresentation occurs, or recurs, following induction, it may prove impossible to correct it by external version due to the loss of liquor and delivery must then depend upon internal version or Caesarean section. Gibson (1952) severely criticizes the policy of correcting the unstable lie and releasing the liquor, and it is certainly true, as he claims, that this offers no guarantee that the correct presentation will persist. Of 47 cases induced because of an unstable lie, 42 were delivered vaginally, only one baby failing to survive. In the other 5 cases Caesarean section was performed because of recurrence of the malpresentation (3 cases), prolapsed cord (1 case), and accidental haemorrhage with foetal distress (1 case). On one occasion the recurrence of a transverse lie was not detected early and the baby though extracted alive, failed to survive.

While our results are not so bad as those which Gibson quotes, these patients gave rise to much anxiety, and the writer agrees that the policy of induction for malpresentation is generally undesirable. It is preferable, though not always practicable, to have these patients under observation in hospital prior to their expected date of delivery, and to allow labour to start spontaneously.

Discussion

Gibson (1952) in his survey of surgical inductions regarded an incidence of 9·9 per cent

of all deliveries at the Royal Maternity Hospital, Belfast, as "high". A search through maternity hospital reports of that time largely confirms his view. The figures then appeared to range from 2·3 per cent (National Maternity Hospital, Dublin) to 10·5 per cent (Glasgow Royal Maternity Hospital). The chief indication in most British centres was pre-eclampsia; it accounted for 62 per cent of inductions in the series of Drew Smythe (1949) and 75 per cent of the inductions in Belfast. Thus British practice in relation to surgical induction could at that time be termed conservative, reflecting a belief that the procedure was not without risk.

When Tennent and Black (1954) published the results of 1,585 inductions, their induction rate was notably higher (18·3 per cent). Their chief indication was prolongation of pregnancy and this departure was noted in a leading article of the *British Medical Journal* (1954) as a step "in accord with the results of recent research, academic and clinical, on the perils of prolonged pregnancy". They encountered very few difficulties, their results were good and it was inferred that the risks described in the past could be largely avoided. However, Evans (1954), reviewing 843 inductions at Guy's Hospital covering a 25-year period, continued to attribute much morbidity and some mortality, maternal and foetal, to the procedure. In reply to some criticism, he showed that the hazards were as common in the later as the earlier years of his report and stated that other series showing better results were largely those including "elective induction", the most favourable group of cases.

The present report comes from a hospital dealing with a large volume of abnormal midwifery. A study of the indications will show that there are fewer "normal" (prolonged pregnancy) cases than in Tennent's series, but when compared with the Belfast figures there are many more non-toxaemic indications and, broadly, this series appears to be most comparable with that from Guy's Hospital. Of course, an induction rate of 19·8 per cent of all deliveries must carry the inference that, at this centre, the procedure of induction has been regarded as being largely free from undue risk and the present survey was undertaken to examine the truth of this.

In brief, this study shows that surgical induction will not always prove as trouble-free a procedure as Tennent and Black (1954) suggest. But the difficulty encountered has not been nearly as great as that reported by Evans (1954) in a seemingly comparable group of cases.

For the mother, sepsis has always been the chief hazard. In this series it is noted that, *provided delivery is subsequently accomplished normally*, there is a low rate of notifiable (genital) pyrexia (1·4 per cent compared with an overall figure for all hospital cases of 2·7 per cent). When induction is followed by Caesarean section the pyrexia rate rises to 9·8 per cent. In both maternal deaths, sepsis present at the time of an operative delivery may have been an aetiological factor, and 2 similar cases are recorded by Gibson (1952). Tennent's only death also occurred when Caesarean section followed induction. Therefore in such cases there is much to be said for a protective antibiotic "umbrella" as recommended by Lemmon (1948).

Further study is required to decide whether surgical induction itself tends to cause a raised incidence of operative deliveries. If it were proved to do so, then such a policy as "elective induction" on the grounds of convenience, described by American writers (e.g., Erving and Kenwick, 1952) would be open to serious criticism. The advent of the pitocin drip should of course reduce the incidence of subsequent Caesarean section quoted in the present report.

Foetal mortality attributable to the induction can be kept to a low figure if placental separation is avoided. The high incidence of cord prolapse recorded by Evans (1954) has not been repeated in this series and still less trouble is reported by Gibson (1952) and Tennent and Black (1954). It is accepted that a prolonged interval between induction and delivery must increase the foetal risk. Our delay has been somewhat longer than most, but it is thought that this can be reduced by concentrating on forewater rupture and, where necessary the use of oxytocin by the intravenous route. Valid comparisons of foetal loss are of course impossible, for foetal mortality must be related to the amount of "abnormal

material" in each individual group of cases. Therefore attributable foetal loss only has been emphasized.

Summary

The results of 1,099 surgical inductions are presented.

There were 4 maternal deaths; surgical induction may have been a contributing factor in 2 deaths, through the introduction of infection.

Maternal deaths due to sepsis in this and in previous reports have occurred when operative delivery has been undertaken following induction and in such cases prophylactic chemotherapy may be indicated. Sepsis is otherwise not a serious hazard.

Twelve foetal deaths were attributable to the induction. The chief factors responsible were placental separation, prolapse of the cord, subsequent malpresentation and intra-uterine infection.

Unsatisfactory results are especially liable to follow surgical induction in cases with hydramnios and an unstable presentation. For hydramnios, paracentesis abdominis is to be preferred; for the unstable presentation, non-interference in hospital.

It is suggested that there may be an increased incidence of inertia and disordered uterine action following induction, and therefore an increased Caesarean section rate. At least on these grounds, elective induction seems open to criticism.

Sixty per cent of the women induced were in labour within 24 hours and 80 per cent within 48 hours. Seventy per cent were delivered within 48 hours.

With the possible exception of pre-eclampsia, the delay between induction and the onset of labour (or delivery) did not alter appreciably in relation to different indications. There was no difference in the delay in primigravidae as opposed to multigravidae and surprisingly little variation at different periods of gestation, in this series of cases.

Acknowledgments

I should like to thank the Consultant Staff of the Birmingham Maternity Hospital for permission to publish this report. It would not have been possible without the careful records kept by the Resident Surgical Officers, 1950–52, Messrs. R. R. Trussell, J. B. Farquhar and R. G. H. Hall to whom I wish to record my debt.

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PREGNANCY IN DIABETIC WOMEN

An Analysis of a Series

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IN the modern treatment of diabetes mellitus with insulin the aim of the physician is to allow the diabetic woman to lead a normal life which includes the bearing of children. Before 1923 amenorrhoea and infertility were common in diabetic women, and pregnancy was rare and often fatal both to mother and baby, but, since the control of the disease with insulin, it is possible that otherwise healthy diabetic women are as fertile as non-diabetic women. However, the problem of determining the most effective management of the diabetic pregnancy is difficult because the series reported by most centres have necessarily been small, diabetes mellitus being a relatively infrequent disease in the younger age groups. Joslin's (1946) figures for America show that about 1 person in 1,000 in the childbearing age is diabetic. The incidence of pregnancy associated with diabetes mellitus after 1923 is variously reported. Gilbert and Dunlop (1949) quoted 70 diabetic pregnancies in 20,438 deliveries, approximately 1 in 292. Sheumack (1949), in Sydney, reported 45 viable pregnancies in 38,611 deliveries, or 1 in 858. Peel and Oakley (1949) noted an incidence at King's College Hospital of 1 in 50. The figures vary according to the presence or otherwise of a diabetic clinic in the hospital, and the size of the clinic. At St. Thomas's Hospital, London, where 7,680 deliveries have occurred in the last ten years, there have been 30 viable pregnancies in diabetic women, an incidence of 1 in 256. This figure, of course, does not indicate the fertility of diabetic women as a group.

It was considered of interest to examine a series of cases where the diabetes mellitus had been treated by the "free diet" method, to determine if this had any apparent effect on the maternal or foetal mortality or on the incidence of toxaemia in pregnancy. Unfortunately this series is not a large one from a statistical point of view. It comprises 51 pregnancies reaching viable age since 1940, in 29 women with diabetes mellitus, who attended the diabetic clinic at St. Thomas's Hospital regularly and who all, with one exception, were known to suffer from diabetes before the pregnancy began.

Each patient was supervised at the antenatal clinic as soon as pregnancy was diagnosed, usually before the 12th week, following which the women attended both the diabetic and antenatal clinics regularly at least every two weeks, and more often if necessary. The management of pregnancy, labour and puerperium was conducted by a team consisting of an obstetrician, a physician and later a paediatrician. All cases required insulin throughout pregnancy or in the 2nd or 3rd trimesters and this was given either as soluble insulin or as one of the long acting preparations found to be suitable for the individual patient. All patients were changed to soluble insulin at the time of delivery or in the event of any surgical procedure involving a general anaesthetic. The composition of diet was largely left to appetite and except in cases of obesity no restriction was placed on the patients' caloric intake or on the form in which carbohydrate foods were taken. It was found that with this method the day-to-day caloric value of the diet tended to remain fairly constant (Goadby, 1950). The importance of regular meal hours was stressed.

At each visit a noon blood sugar estimation was done, the aim being to keep this reading as far as possible within 100 mg. ±20 mg. per cent whilst avoiding insulin reactions. Glycosuria in the first morning specimen was ignored unless it were associated with ketonuria.

On the obstetric side, each case was treated individually, delivery by Caesarean section not being automatically advised in primiparae. The question of delivery is considered later.

Oestrogens and progesterone were not used.

Analysis of Figures

Maternal Complications

Mortality

There were no maternal deaths in this series. The common causes of maternal mortality, eclampsia and diabetic coma, can be avoided by strict antenatal supervision.

Abortions

As far as can be ascertained, the spontaneous abortion rate in pregnant diabetic women in this series was about 22 per cent, which is approximately double the usually expected figure for non-diabetic women. These figures must, of course, be regarded with some reserve. There is considerable divergence in the quoted figures in the literature, estimates varying between 8 and 22 per cent (Table I).

Table I
Abortion Rates

Author	Diabetic Women (Per cent)
Barns and Morgans (1948)	14
Barns and Morgans (1949)	10·9
Rolland (1954)	<8
Sheumack (1949)	22·2
Given *et al.* (1950)	13
White and Hunt (1943)	15
	Non-Diabetic Women
Barns and Morgans (1948)	11·8

Toxaemia of Pregnancy

Of the 51 pregnancies, 21 or 41 per cent showed pre-eclamptic toxaemia and 1 had hypertension alone, a total of 43 per cent. The criteria of diagnosis for pre-eclampsia were a blood pressure exceeding 140/90 mm. of mercury and either albuminuria (19 cases out of 21) and/or oedema. There were no cases of eclampsia. Against an incidence of pre-eclamptic toxaemia in non-diabetic women of 9·3 per cent at St. Thomas's Hospital, that in pregnant diabetic women was more than 4 times as great. One-third of the multiparous women and one-half of the primiparous had pre-eclampsia (see Table II).

In 2 women pregnancy had to be terminated, one at 28 weeks, the other at 29 weeks for severe pre-eclampsia, although both were receiving treatment in hospital. In the case of the latter patient, her first pregnancy ended in a spontaneous premature labour at 30 weeks following an ante-partum haemorrhage and intra-uterine death during an attack of diabetic ketosis; diabetic control had been unsatisfactory throughout, the patient having had several ketotic attacks earlier in the pregnancy. Her second pregnancy had to be terminated at 29 weeks by Caesarean section for severe pre-eclampsia despite improved diabetic control. In the one patient in whom hypertension alone developed, foetal intra-uterine death occurred in two pregnancies, the first at 32 weeks, the other later in pregnancy resulting in the birth of a macerated foetus weighing 4 pounds 7 ounces. In only 2 patients with toxaemia did the albuminuria persist after discharge.

Comparison with other series is difficult because of differing diagnostic criteria (Table III). Barns and Morgans (1949) reported a pre-eclamptic incidence of 43 per cent, the rate for non-diabetic women being 35 per cent. On the other hand Peel and Oakley (1949) at King's College Hospital had a diabetic pre-eclamptic rate of 10·7 per cent, and in a large questionnaire series, 18·9 per cent. In both of these latter series the foetal loss in the presence of toxaemia was about 45 per cent, the overall foetal loss in each being 24·9 per cent and 40·3 per cent respectively.

These figures raise the question, is the high foetal mortality rate associated with the high incidence of toxaemia? Brosset and Werkö (1950) in Stockholm found no relation between foetal death and toxaemia, nor did Lawrence and Oakley in 1942. However, in our experience,

TABLE II
Incidence of Toxaemia and Hydramnios

	Diabetic	Multiparae	Primiparae	Foetal Loss	Non-diabetic
No. of pregnancies	51	30	21	15	3,930
No. of cases of toxaemia	22 (43 per cent)	11	11	8	366 (9·3 per cent)
No. of cases of hydramnios ..	17 (33 per cent)	10	7	3	?

TABLE III
Incidence of Toxaemia of Pregnancy

Author	Incidence of Toxaemia (Per cent)	Remarks
Barns and Morgans (1949)	43	Pre-eclampsia. Rate in non-diabetic women 35 per cent
Lawrence and Oakley (1942)	10·2	Albuminuria with hypertension and oedema
Medical Research Council (1955)	20–23	Albuminuria
	14–25	At least two of hypertension, albuminuria, oedema
Peel and Oakley (1949) K.C.H. ..	10·7	Pre-eclampsia
Q.	18·9	
Reis *et al.* (1950)	10	Hypertension and albuminuria
Sheumack (1949)	44·5	Pre-eclampsia
Given *et al.* (1950)	46	All toxaemias
	33	Hypertension
White (1949)	50	Hormonal imbalance present
	5	Normal hormonal balance
White and Hunt (1943)	42	Hypertension and/or albuminuria (no hormones given)

even in pregnancies without diabetes, the presence of toxaemia increases the foetal mortality (and *see* Brash, 1949). In the diabetic woman the occurrence of pre-eclampsia constitutes a strong argument in favour of inducing labour. In this series 8, that is roughly half of the foetal deaths, were associated with toxaemia, intra-uterine death occurring in 6 cases, the resulting macerated foetuses weighing only 5 pounds in 2 cases and less than 5 pounds in the remaining 4. The other 2 deaths were neonatal ones at about 30 weeks, Caesarean section having been performed for severe pre-eclampsia. Significantly, in all cases of intra-uterine death but one, toxaemia was present. Again in the presence of toxaemia the viable foetal wastage was 36·4 per cent, whereas in non-toxaemic cases the loss was 24·2 per cent.

In our opinion the question of toxaemia occurring in the diabetic pregnancy is a vital one, and will be considered later in the section under Management and Labour.

Hydramnios

There is no general agreement in the literature as to the frequency of hydramnios in diabetic pregnancies largely because the estimation of excess amniotic fluid depends on clinical impression (Table IV). Hydramnios of sufficient

TABLE IV
Incidence of Hydramnios

Author	Rate (Per cent)
Barns and Morgans (1949)	29
Medical Research Council (1955) ..	40
Peel and Oakley (1949) K.C.H. ..	30·5
Q.	26·8
Sheumack (1949)	11
Given *et al.* (1950)	"as in non-diabetic women"

degree to cause respiratory embarrassment or other pressure symptoms did not occur in this series and no cases required interference for the

hydramnios *per se*. The diagnosis of lesser degrees of hydramnios was not made unless the presence of excessive liquor was noted by at least two independent observers. Seventeen cases out of 51 had hydramnios, an incidence of 33 per cent, and in 7 of these toxaemia of pregnancy was associated (Table II).

Hydramnios was associated with only 1 case of the 3 in which congenital abnormalities occurred. The birth weight of babies of different maturities was not significantly higher in cases of hydramnios than in those without hydramnios but the numbers are small.

It did not seem that the use of an unprescribed diet had any significant effect on the incidence of hydramnios which was virtually the same in this series as in others using a strict diet.

Puerperium

Diabetic patients appear no more liable to puerperal obstetric complications than normal mothers. No difficulty was found with wound healing and the puerperal pyrexia rate was not increased above that occurring in non-diabetic women.

Diabetic Complications

Insulin requirements rose during the 2nd and 3rd trimesters in 82·5 per cent of cases, remained unchanged in 12·5 per cent and fell in only 5 per cent. With this frequent rise mild ketonuria was not uncommon in the later stages of pregnancy. In 2 cases a state of considerable insulin resistance became established, which disappeared in one case within 72 hours after Caesarean delivery but continued in the other case for more than two months after confinement. In most cases insulin requirements fell rapidly in the first 24 hours post-partum, and unless this was anticipated by lowering the insulin dose, hypoglycaemic reactions were common. In 75 per cent of cases the insulin requirements returned to pre-pregnancy levels soon after delivery. In 17·5 per cent insulin requirements two months post-partum were higher than previously and in 7·5 per cent lower.

With the supervision of the diabetes as described above, little difficulty was encountered because of variations in renal threshold and it was not found necessary to determine any patient's threshold during pregnancy. The most commonly reported change is a fall in the threshold during the 3rd to the 5th months (Lawrence and Oakley, 1942; Peel and Oakley, 1949). Lambie (1926) stated that in the 6th and 7th months 45 per cent of women have lowered renal threshold for glucose.

FOETAL COMPLICATIONS

Foetal wastage occurred in 15 of 51 viable pregnancies, i.e., those over 28-weeks maturity —a percentage loss of 29·4 per cent (Tables V and VI).

TABLE V
Foetal Wastage

	Total	Multi-parae	Primi-parae
No. of viable pregnancies	51	30	21
Viable foetal loss	15 (29·4%)	7	8
Intra-uterine deaths, macerated foetus ..	7	3	4
Fresh stillbirths	3	2	1
Neonatal deaths	3	2	1
Hysterotomies (for toxaemia)	2	0	2

TABLE VI
Foetal Loss Rate

Author	Loss Rate Whole Pregnancies (Per cent)	Loss Rate Viable Pregnancies Only (Per cent)
Barns and Morgans (1948) ..		50
Barns and Morgans (1949) ..		55
Gilbert and Dunlop (1949) ..	51·4	
Lawrence and Oakley (1942) ..	37	
Medical Research Council (1955)		25
Peel and Oakley (1949) K.C.H.		48
Q. ..		40–45
Rolland (1954)	28·6	22·5

Seven intra-uterine deaths occurred, all except one, as mentioned previously, occurring in women with toxaemia. The resulting macerated foetus in 6 cases weighed 5 pounds or less, so that in these toxaemic cases 6 intra-uterine deaths occurred probably before the 36th week. This

high incidence of intra-uterine death early in the last trimester associated with toxaemia, is rather surprising. In larger series it has been shown that the intra-uterine death rate tends to increase in the last 6 weeks of pregnancy and that this death rate becomes higher in the last 4 weeks than does the neonatal mortality due to prematurity (Peel and Oakley, 1949, Q series). This conclusion is not shared by Barns and Morgans (1952), nor does it seem to be borne out by the smaller King's College Hospital series quoted by Peel and Oakley (1949).

Of the 3 fresh stillbirths, 2, one at 39 weeks and one at 37 weeks, were due to foetal death in a prolonged first-stage of labour and might have been averted by timely Caesarean section. The third stillbirth occurred during a breech delivery at 38 weeks in a multipara. These stillbirths account for 3 of the 4 foetal deaths occurring in the last four weeks of pregnancy (see Table VII). The fourth death was an intra-uterine one at forty weeks in the absence of toxaemia.

All 3 neonatal deaths occurred in babies with congenital abnormalities; one with tracheo-oesophageal fistula, cirrhosis of the liver and gross oedema, one with absence of body and tail of pancreas, and the third with a cleft palate and gross exomphalos. The cause of death in the first two cases may have been respiratory as death occurred in the first 48 hours and in the second baby autopsy showed that the air passages were clear but there was partial collapse of the respiratory tissue. In this case death occurred suddenly after 24 hours.

The two cases where Caesarean section was necessary for severe toxaemia resulted in babies twenty-eight weeks old which, not surprisingly, did not survive.

Time and Method of Delivery

As some of the cases in this series dated back more than ten years, no consistent policy regarding time and method of delivery was followed (Tables VII and VIII). No significant tendency to spontaneous premature labour was seen and apart from one case at thirty weeks the smallest baby resulting from spontaneous labour weighed 6 pounds. The method of delivery is of considerable importance in lowering the foetal wastage because of the greatly increased toxaemia rate in diabetic women with a tendency to early intra-uterine death, because of the rising intra-uterine death rate reported elsewhere in later pregnancy and because the large hydraemic immature diabetic foetus tolerates the strain of labour poorly.

In all primiparae and in multiparae with a bad obstetric history or where obstetric complications have arisen, such as prolonged first stage of labour or malpresentation, Caesarean section at the 36th–37th week is advisable.

On the other hand, in multiparae who have not previously had a foetus die *in utero*, who have a favourable obstetric history with relatively easy normal labours and who show no or minimal evidence of toxaemia, termination of pregnancy by medical or surgical induction at about thirty-seven weeks is probably wise. In the absence of toxaemia one is tempted to allow pregnancy to proceed to thirty-eight weeks to reduce the risks of prematurity. This may be justifiable if further work confirms the impression that toxaemia is the important factor in intra-uterine deaths.

This early termination of pregnancy is only justifiable if facilities are available for expert supervision of the premature baby.

The appearance of toxaemia during a diabetic

Table VII

Showing Approximate Time of Termination of Pregnancy, Size of Baby and Temporal Distribution of Foetal Loss

Maturity at delivery (weeks)	40	39	38	37	36	35–30	Under 30
Total No. of pregnancies	9	8	9	8	5	9	3
Average weight in pounds	8–11	8–4	7–3	7–8	6–14	4–14	2
Spontaneous onset of labour	4	2	–	2	1	1	–
Foetal deaths	1	1	1	1	–	5	3
Intra-uterine deaths	1	–	–	–	–	5	1
Fresh stillbirths	–	1	1	1	–	–	–
Neonatal deaths	1	–	1	–	1	–	2

TABLE VIII
Mode of Delivery and Foetal Loss

51 Pregnancies	Caesarean Section	Surgical Induction of Labour	Spontaneous Onset of Labour	Medical Induction for Intra-uterine Death	Hysterotomy for Toxaemia
Total No.	15	21	10	3	2
Multiparae	10	12	6	1	1
Primiparae	5	9	4	2	1
Neonatal and foetal mortality	2	6	2	3	2
Cause of death	1 stillbirth at 39 weeks. 1 neonatal death.	2 deaths in 1st stage of labour. 1 stillbirth breech. 2 macerated intra-uterine deaths. 1 neonatal death.	1 intra-uterine death due to ante-partum haemorrhage at 30 weeks. 1 neonatal death.		2 neonatal deaths. Foetus 28–30 weeks maturity.

pregnancy requires the patient's immediate admission to hospital and careful observation (*see* Hamlin, 1952). If toxaemia persists or increases in severity, then termination must be seriously considered and is indicated as an immediate measure if the foetus has reached a reasonable maturity.

The past history of the patient must also influence any decision taken in the termination of the pregnancy. One patient who had a history of 4 intra-uterine deaths all occurring at about the 32nd week, was delivered by Caesarean section of a live child at 33 weeks. The birth weight of the baby was 3 pounds 4 ounces, but it survived and did well.

Radiological study of the foetus before Caesarean section will detect some congenital abnormalities and avoid an unnecessary operation. There will be a few cases where Caesarean section will result in the birth of a child with considerable congenital abnormalities not radiologically detectable.

Peel and Oakley (1949) stated that delivery by Caesarean section was justified in all primiparae with diabetes and that there should be no hesitation in delivering multiparous patients by Caesarean section who have already had a surgical induction and where labour does not begin or if there is undue delay. It was also pointed out that prolonged labour not only endangers the foetus but is also dangerous to the mother since the diabetic state becomes more difficult to control. In P. White's series in 1949, 68 per cent of the women were delivered by Caesarean section. Given, Douglas and Tolstoi (1950) suggested that induction and vaginal delivery should be preferred but, in the event of unsuccessful induction or prolonged labour, delivery by Caesarean section should be performed.

In this series all Caesarean sections but one were performed under general anaesthetic. Various anaesthetic agents were used, Pentothal being given in 3 cases. In one operation performed under local anaesthesia with caudal block, classical Caesarean section had to be done as relaxation was not sufficient to allow delivery through a lower segment incision.

MANAGEMENT OF THE NEW BORN BABY

The new born babies of diabetic mothers behave, regardless of birth weight, like premature infants and require similar skilled care in a fully equipped centre. It follows that the delivery of a diabetic woman should only take place where such facilities for neonatal care are available.

In the management of the newborn in this hospital, the air passages are cleared at delivery and the babies are placed in inclined cots with their heads low. No glucose is given either by mouth or parenterally (*see* Komrower, 1954), and with this treatment there have been no hypoglycaemic reactions in the infants. The babies are starved for twenty-four hours and then breast feeding, where possible, is encouraged, but skilled nursing attention is necessary as it is found that babies of diabetic mothers, even of 39 or 40 weeks maturity, are lethargic and slow to suck. Tube feeding is frequently necessary. Furthermore, lactation is often inadequate in the diabetic mother and fails to become established, so that in the majority of cases complements and then full artificial feeding become necessary. Toxaemia itself may have an adverse effect on lactation (Brash, 1949).

Discussion and Conclusions

Several points of interest emerge from this analysis. The abortion rate in diabetic women, as far as can be ascertained in this series, is higher than in non-diabetic women.

The toxaemia rate was high and toxaemia tended to appear early in the last trimester. Where intra-uterine death occurred, it occurred mostly between the 28th and 36th weeks (6 cases out of 7), and was almost invariably associated with toxaemia. As the toxaemia factor was associated with more than 50 per cent of the total foetal wastage, then any measure which reduces the incidence of toxaemia should reduce the foetal loss. The shorter the time that the foetus is allowed to spend in a toxaemic diabetic environment, it seems, the better, and the risks of prematurity have to be weighed carefully against this, taking the history of previous pregnancies into consideration in the individual case.

The value of oestrogens and progesterone in reducing the incidence of toxaemia and improving foetal survival rates (White, Koshy and Duckers, 1953) was not established by the M.R.C. trial (1955).

Another line of treatment requiring investigation is the dietetic one using the restriction of salt and caloric intakes, which method has been used in some centres (Sheumack, 1949; Hamlin, 1953). Possibly the high toxaemia incidence in the present series may be due in part to unrestricted caloric intake which in this particular group of women tended to be in the form of carbohydrate. This explanation, however, is obviously not entirely satisfactory.

As with hydramnios the degree and persistence of glycosuria did not alone seem to account for the high toxaemia rate. While in some cases toxaemia occurred where the control of blood sugar levels was generally unsatisfactory during pregnancy, this was by no means always the case and in many patients severe toxaemia occurred despite good control of the diabetes.

The time of termination of pregnancy has been considered and the method should be one which places the least physical strain on the foetus, compatible with maternal safety. Radiological study of the foetus before Caesarean section should be done invariably.

As regards maternal diabetes, the avoidance of ketotic and hypoglycaemic attacks of any duration is essential and as toxaemia may be associated with unsatisfactory diabetic control, the latter should be strict with the object of minimizing at least the risk of toxaemia. Where strict control of glycosuria is attempted, the lowered glucose renal threshold of later pregnancy must not be forgotten. In 80 per cent of cases the insulin requirements rose in the 2nd and 3rd trimesters, but fell immediately on delivery, the risk at this time being hypoglycaemia.

The foetal mortality in this series seemed to bear no relationship to the severity or duration of the mother's diabetes. All the multiparous women who lost babies had unfortunate previous obstetric histories, whereas in the 23 successful pregnancies in multiparae, only 7 had had a previous stillbirth or intra-uterine death and only 2 of these 7 women gave a history of a foetal death on more than one occasion.

Skilled care of the newborn is imperative even where the baby is of average normal weight.

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THE RUPTURED CAESAREAN SECTION SCAR

BY

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IN the literature on pregnancy and labour following Caesarean section the general opinion has been expressed that the lower segment scar is less likely to rupture than the classical one. Eames (1953), quoting the collected results of five authors favouring vaginal delivery after Caesarean section, gives the figures of 1·3 per cent for ruptures of lower segment scars in subsequent pregnancy and labour, and 2·6 per cent for classical scars. Lawrence (1953) gives figures of 0·47 per cent of ruptures of the lower segment scar in all subsequent pregnancies, and 0·65 per cent for cases subjected to a minimum of 3 hours labour; the comparable figures for the classical scar being 1 per cent and 2·2 per cent respectively. Furthermore, it has generally been held that, should the uterus rupture, the scar in the lower segment is less likely to do so explosively, the clinical picture being less severe than when the classical scar gives way.

It is surprising, therefore, to find that Lane and Reid (1953) discovered at elective repeat Caesarean section 3·3 per cent of scar rupture in 426 patients who had previously been delivered by lower segment Caesarean section compared with 2·2 per cent of rupture in 246 patients with previous classical scars. It is disturbing to read their conclusions that the classical incision is more likely to withstand the forces of labour than the lower segment one, and that surgical management of a patient with a ruptured classical scar is much less difficult and poses fewer problems than in a patient with lower segment scar rupture. Eastman (1954) holds a similar view since he warns us that, if one of these lower segment scars does rupture, the maternal mortality attributable to the accident is much higher than in rupture of the classical scar.

As these statements were not in accordance with my own experience, nor as it seemed with that of some other authors, it was resolved to examine the literature on this subject more closely to see if evidence could be found to clarify the picture. To determine the incidence of both forms of scar rupture an examination was made of all reported series dealing with pregnancy and labour after Caesarean section in the British Isles in recent years; these results are reported here. To investigate further the severity of the different forms of rupture as many cases as possible of ruptured, classical, or lower segment scars reported in the literature in English during the 10-year period 1946–January 1956 were examined, and an analysis was made of all in which some clinical details, or at least the maternal and foetal mortality, were given. These results are reported also. During this analysis, several important differences have been noted in the clinical features of ruptured classical and lower segment scars, which will finally be described.

INCIDENCE OF SCAR RUPTURE

In recent years six series of cases dealing with pregnancy and labour following Caesarean section have been published from the British Isles (Browne, 1951; Lawrence, 1953; Bruce, 1953; Winchester and Brown, 1954; Baker, 1955; Dewhurst, 1956), and an analysis of the collected information they contain has been made in Table I. The total cases number 762 viable pregnancies following classical Caesarean section and 1,530 viable pregnancies following lower segment Caesarean section; 17 cases of ruptured classical scar occurred, and 8 of ruptured lower segment scar. The numbers have been broken down further into those in which elective Caesarean section was performed, those which were in labour, and those delivered

TABLE I

Author	Total		Elective Caesarean Section		In Labour		Vaginal Delivery		Ruptured Scars	
	Classical	Lower Segment	Classical	Lower Segment	Classical	Lower Segment	Classical	Lower Segment	Classical	Lower Segment
Lawrence (1953)	400	449	222	139	178	310	74	121	4	2
Browne (1951)	16	76			16	76	16	76		1
Baker (1955)		100		17		83		74		1
Dewhurst (1956)	84	635	44	283	40	352	31	235	7	3
Bruce (1953)		41				41		34		
Winchester and Brown (1954)	262	229					69	112	6	1
Total	762	1,530	266	439	234	862	190	652	17	8

vaginally, except that in the figures quoted by Winchester and Brown the numbers in labour and delivered by elective Caesarean section are not known, but simply those delivered by Caesarean section, whether in labour or not. The frequency of rupture of both forms of scar has been calculated and has been expressed as a percentage of (*i*) the total, (*ii*) those in labour (omitting Winchester's figures), (*iii*) those in which vaginal delivery took place; for the classical Caesarean section the figures are 2·2 per cent rupture of all cases, 4·7 per cent of those in labour, and 8·9 per cent of those delivered vaginally, whilst for lower segment Caesarean section the comparable figures are 0·5 per cent, 0·8 per cent, and 1·2 per cent.

THE SEVERITY OF THE ACCIDENT

It has been possible to obtain from the literature reviewed for the period under consideration information on maternal mortality in 100 cases of ruptured classical scar, and 55 of ruptured lower segment scar, and on foetal mortality in 82 and 48 such cases respectively (Flint, 1947; Marks, 1948; Vartan, 1948; Hindman, 1948; Karsh, 1949; Fitzgerald, Webster and Fields, 1949; Lawrence, 1949, 1953; Brierton, 1950; Watt, 1950; Dewhurst and Rowley, 1951; Cosgrove, 1951; Parker and Jones, 1951; Schmitz and Gajewski, 1951; Wilson, 1951; Browne, 1951; Parsons, 1952; Love, 1952; Bruce, 1953; Winchester and Brown, 1954; Pickles, 1955; O'Dwyer, 1955; Baker, 1955; Coleman, 1955; Wolfson and Lancet, 1955; Bak and Hayden, 1955; Feeney and Barry, 1956; Voogd, Wood and Powell, 1956). Details of maternal mortality are given in Table II, from which it will be seen that 5 mothers were lost in the 100 with a ruptured classical scar, whilst all 55 mothers survived

TABLE II
Maternal Mortality

	Total	Maternal Deaths
Classical scar	100	5
Lower segment scar	55	0

TABLE III
Foetal Mortality

	Total	Stillbirth or Neonatal Death	Living Child
Classical scar ..	82	60	22
Lower segment scar	48	6	42

rupture of the lower segment scar. Table III shows a foetal mortality of 60 (73 per cent) of 82 babies in cases of classical scar rupture, and only 6 (12·5 per cent) of 48 with lower segment scar rupture.

An attempt was next made to grade the severity of the accident into three categories: (*i*) those without any symptoms at all, the findings being purely accidental, (*ii*) those with clinical features pointing to rupture of the scar without material deterioration in the mother's condition, and (*iii*) those where shock and collapse were present; sufficient clinical details were obtained from 38 case reports in each type of scar. These show (Table IV) that, whilst 5 ruptured classical scars were discovered by accident, 8 presented with features without collapse occurring, and 25 patients were in a state of shock, the ruptured lower segment scars showed 18 accidental findings, 17 with clinical signs not amounting to collapse, and 3 only with collapse evident.

TABLE IV
Severity of Symptoms

	Total	No Symptoms	Symptoms No Collapse	Collapse
Classical Scar	38	5	8	25
Lower segment scar	38	18	17	3

One specially dangerous form of scar rupture being that which occurs suddenly before labour or even some time before term, an attempt was made to compare the frequency of this in the two groups. Table V shows that, in well over

TABLE V
Time of Rupture of Scar

	Total	Not in Labour	In Labour
Classical scar ..	86	49	37
Lower segment scar	45	11	34

half the cases of classical scar rupture and a quarter of those of lower segment scar rupture, the patient was not in labour when the accident occurred. Further examination of these cases shows, furthermore (Table VI), that, of 19

TABLE VI
Clinical Rupture Before Labour

	Total	Accidental Finding	Clinical Rupture
Classical scar ..	19	3	16
Lower segment scar	11	9	2

classical scar ruptures before labour, 16 had clinical signs of rupture calling for urgent treatment, whilst, in 11 cases of lower segment scar rupture, 2 only gave rise to clinical features suggesting that rupture had occurred, and 9 were simply accidental findings at Caesarean section.

CLINICAL FEATURES OF LOWER SEGMENT SCAR RUPTURE

Examination of the clinical details given in the 38 cases of both forms of ruptured scar shown in Table IV made it clear that, whilst many cases of ruptured classical scar presented with typical features of scar rupture—severe abdominal pain, cessation of uterine contractions if in labour, collapse, tenderness, altered shape of the abdomen with the foetus palpable beneath the abdominal wall, and absent foetal heart sounds—the majority of cases of lower segment scar rupture did not present these features. Often one or two signs only were present to suggest that rupture had occurred. Pain and tenderness low in the abdomen and mainly over the old scar were the most constant features, pain apart from uterine contractions being present in 9 cases, and tenderness in 11. Five cases had haematuria, a significant sign indicating coincident bladder rupture, and uncommon in cases of ruptured classical scar—further reference will be made to this in a case described below. Three cases only had vaginal bleeding; in 2 a defect was palpable in the lower segment, and in 2 foetal parts could be felt with ease beneath the abdominal wall, although the foetus was still *in utero*. In 3 others there was bulging of the membranes through the tear, recognizable as a lower abdominal swelling. In 3 cases only collapse occurred. A significant feature was that in most cases uterine contractions persisted despite the rupture being present. In general, the progress of the tear was less rapid and the deterioration in the patient's condition much less marked than in cases of classical scar rupture, although a serious clinical picture could develop if the early signs were not recognized. A case described by Brierton (1950) illustrates this well. After his patient had been in labour for 1½ hours she developed constant suprapubic pain; after 3½ hours, tenderness in the old scar; after 4½ hours a defect was palpable abdominally, and normal delivery occurred 1 hour later. Symptoms of internal bleeding followed, and, at laparotomy, a tear 8 cm. long was discovered in the lower segment, and nearly one pint of blood was present beneath the peritoneum. The early signs of rupture cannot,

however, often be ignored with such impunity, as, although the extension of the tear may be fairly slow and bleeding fairly slight whilst still confined to the scar, extension laterally into the uterine vessels can give rise to severe bleeding and shock. A case not previously recorded is described below, which illustrates the different type of clinical picture presented by rupture of the lower segment scar as compared with ruptured classical scar, and which shows also the importance of haematuria in the diagnosis which had in fact been suspected here before the blood-stained urine was discovered.

Case Record

Mrs. S. was delivered by lower segment Caesarean section in her first pregnancy of a baby 8¼ pounds weight for foetal distress during labour. In her second pregnancy in 1954 she was admitted near term, and the membranes ruptured spontaneously on the 2nd November, 1954, regular strong contractions following. The head was entering the brim but was not engaged. After labour had been in progress 5 hours, tenderness in the suprapubic area developed, and there seemed to be some ballooning of the lower uterine segment, although regular uterine contractions persisted. Early uterine rupture was suspected, and as the labour was not progressing well the patient was taken to the operating theatre, where catheterization obtained 2 ml. of pure blood. At laparotomy an incomplete rupture of the lower segment at the site of a previous scar was discovered. The foetus was still *in utero*, the shoulder visible through the loose peritoneum of the utero-vesical pouch. The child was extracted after opening the peritoneum and extending the hole in the uterus. The child weighed 9 pounds 3 ounces and was alive and well. A large, irregular tear in the posterior wall of the bladder was then discovered, about 3 inches in length. After suture of the uterine incision and the bladder tear, the abdomen was closed and the patient made a good recovery.

Discussion

It is clear from these figures that neither the incidence nor the severity of rupture of the lower segment Caesarean section scar is as great as that of the classical Caesarean scar. It is indeed worthy of note that, even when all cases of rupture of the lower segment scar in the six series of cases examined are expressed as a percentage of those cases alone in which vaginal delivery took place, so low a figure as 1·2 per cent is obtained, which makes the figure of 3·3 per cent of scar dehiscence at elective repeat Caesarean section, described by Lane and Reid (1953) even more remarkable. It raises the question, moreover, as to whether an apparent uterine defect seen at Caesarean section before labour is evidence that extension of the "tear" is certain or whether such a uterus would not often withstand the forces of labour without apparent untoward effect. Stabler (1956) holds the view that many of these "windows" in the uterine muscle seen at laparotomy are areas not of rupture but of lack of healing of the original incision. A case described by Donnelly (1951) gives some support for this view for at laparotomy in a patient who had two previous transverse Caesarean section scars a defect was found across part of one scar through which the placenta was emerging and was firmly implanted on to the omentum. It is possible that those cases in which small scar defects are found without any surrounding bleeding are examples primarily of poor wound healing, as Stabler suggests. Whether this view is correct or not, the evidence is overwhelming from these figures that the integrity of the lower segment scar is greatly superior to that of the classical scar.

The less serious clinical picture presented by a ruptured lower segment rather than a classical scar is obvious in terms of mortality alone by the different maternal and foetal deaths in the two groups (Tables II and III), 5 maternal deaths occurring in the 100 cases of ruptured classical scars, all 55 mothers with ruptured lower segment scars surviving, and 73 per cent foetal loss compared with 12·5 per cent. The more serious threat to the mother's life of the classical rupture can be seen in another way when we note that in two-thirds of such cases the patient was collapsed, requiring transfusion and urgent treatment, compared with less than one-tenth of the cases of lower segment rupture. The dangerous complication of sudden scar rupture before labour or even some time before term so noticeable a sequence of the classical scar is seldom observed when the scar is in the lower segment, such cases of ante-partum rupture of the lower segment scar as have been described being in most cases accidental findings at elective Caesarean section, two cases only of clinical rupture having been recorded.

One reason for better maternal and foetal results in lower segment scar rupture has undoubtedly been the slower progress of the

tear and the longer time available in which the diagnosis may be made. Symptoms and signs of this form of scar rupture are however less definite than those of the classical type of upper segment rupture and, unless these differences are appreciated, the diagnosis may not be made until dangerous extension of the tear has occurred. As we have seen, pain and tenderness in the lower abdomen, and especially in the old scar are the most common features. They can, however, be misleading, and it is certain that a number of uterine scars will be found intact if laparotomies are performed on these features alone. Nevertheless, the suspicion of rupture must always be raised by their appearance during labour, or even before, and if good progress of labour is not being made many would consider it wise to interfere lest the scar was indeed beginning to give way. The importance of haematuria has been stressed already and it is amongst the most serious signs calling for urgent treatment. The bulging of membranes through the tear to produce a swelling in the lower abdomen is a most characteristic sign when it appears; it is important to appreciate however that it is an indication not that rupture is imminent, but that it has already occurred.

Lastly, mention must be made of the fact that in the great majority of cases of lower segment scar rupture described in the literature, uterine contractions have continued although the tear was present. As in most cases allowed to go into labour with a previous Caesarean section scar the head is already engaged, or becomes so, early in labour, under these circumstances, unless the scar gives way throughout the full extent and the tear extends still farther, it will be difficult for the uterus to expel the child into the abdomen, and pains will continue. For the same reason, palpation of foetal parts beneath the abdominal wall except in the immediate area of the old scar is a rare finding in this form of rupture.

Whether we view rupture of the uterine scar from the point of view of its incidence or of its severity these figures seem to justify the view that, other things being equal, an attempt at vaginal delivery after a previous lower segment Caesarean section can be made with a considerable degree of safety. This cannot be said for the classical scar for the incidence and severity of its rupture as described here makes pregnancy, let alone labour, so much more of a hazard than after the lower segment operation that the classical operation, except in exceptional circumstances such as those formulated by Russell (1949), should not be performed.

Summary and Conclusions

It has been suggested that contrary to previous opinions the incidence and severity of rupture of a lower segment Caesarean section scar in a subsequent pregnancy and labour is greater than that of the classical scar. In an effort to clarify this picture the incidence of both forms of scar rupture has been studied on the collected figures of 6 series of cases published from the British Isles in recent years, and the severity of the accident has been investigated by examining the reports of cases published in English between 1946 and January 1956.

Neither the incidence nor the severity of rupture of the lower segment Caesarean section scar was found to be as great as that of a classical scar; 17 cases of ruptured classical scar were reported in 762 viable pregnancies, the incidence being 2·2 per cent of all cases, 4·7 per cent of those in labour, and 8·9 per cent of those who delivered vaginally, whilst 8 cases of ruptured lower segment scar were demonstrated in 1,530 viable pregnancies, an incidence here of 0·5 per cent, 0·8 per cent, and 1·2 per cent respectively. Five mothers died out of 100 cases of ruptured classical scar, whilst all 55 patients with ruptured lower segment scar survived, and a foetal mortality of 73 per cent was found for classical scar rupture, compared with 12·5 per cent for lower segment scar rupture. Other evidence of the greater danger of classical scar rupture was found, such as a much higher incidence of shock and collapse and a greater number of antepartum ruptures, many of which called for urgent treatment.

Examination of published case records has shown many differences in the clinical picture of ruptured classical and lower segment scars, and attention has been drawn to these. Instead of the common textbook picture of classical rupture so often seen, one or two features only may indicate that a lower segment scar has given way. The most constant features were pain and tenderness

in the region of the old scar, others being haematuria (indicating coincident bladder tear), vaginal bleeding, palpation of the foetal parts across the tear with the foetus still *in utero* and bulging of membranes through the tear, producing a lower abdominal swelling. Uterine contractions continue despite the tear being present in the great majority of cases.

From the evidence obtained in this survey it is clear that the hazards of pregnancy and labour after classical Caesarean section are far greater than after the lower segment operation, the integrity of the lower segment scar as demonstrated here justifying subsequent vaginal delivery if other favourable circumstances are present.

I am grateful to the Board of St. Mary's Hospitals, Manchester, for allowing me to include the case report described here and to Drs. J. K. Feeney, A. Barry and R. Brown for their help in supplying further information about cases which they had previously reported.

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RECURRENT OBSTRUCTION OF LABOUR DUE TO FOETAL POLYCYSTIC KIDNEY DISEASE

Record of a Case and Review of Literature

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INTRODUCTION

POLYCYSTIC kidney disease is a condition in which there is a massive involvement of the renal parenchyma by cysts varying in number and size.

It is probably always bilateral, and is congenital and familial in nature, being transmitted equally by the male and female sex.

Although the disease is not a common one—its clinical incidence is said to be 1 in 4,000 cases (Higgins, 1952)—post-mortem statistics suggest that it is more common than its clinical frequency would imply. Jensen (quoted by Legrand, 1937) gives an incidence of 1 in 1,700, Higgins (1952) 1 in 500 to 750 births.

It appears either as a disease of the newborn, or as an affliction of adult life, but, whereas in the former it causes immediate death, in the latter it allows survival usually into the second half of life. Because of this fact, and because too the macroscopic appearances are so different in neonate and adult, many refuse to believe that it has the same origin in both. Microscopic study, however, has convinced the majority that they merely represent two stages of the same condition (Lambert, 1937).

The defective mechanism producing congenital cystic kidney disease has not definitely been established, but the best formulated theory is that it is due to failure of fusion between collecting tubules arising from the ureteric bud—the secretory tubules which arise from the metanephros.

In 19 to 28 per cent of cases cystic disease extends to other organs, such as the spleen, liver and pancreas (Jensen, quoted by Legrand, 1937).

CASE REPORT

The following is a report on a case admitted recently to Hull Maternity Hospital, in which recurrent dystocia due to polycystic disease of the kidney of the foetus occurred.

Mrs. D.S., aged 26, gravida-4, was admitted on the 4th July, 1955. Apparently she had always enjoyed good health. The only relevant information in her family history was that her husband's mother was thought to have had a kidney removed at one time.

Previous Obstetric History

(1) 1949. Patient was delivered at term by forceps of a 7 pounds 13 ounces (g. 3,542) male infant. There was some hypertension and oedema present, but no albuminuria, during the antenatal period. The child is alive and well.

(2) 1952. She booked for hospital confinement in view of the difficulty with her previous labour. Nothing abnormal was noted during her antenatal care. She was admitted in the second stage of labour one month before her expected date of confinement, with the head almost born. The abdomen seemed unduly large, and it was thought that she might have twins. The head and shoulders were born, and after this there was no further progress, despite good pains. Examination under anaesthesia revealed the fact that the foetus had a large abdominal tumour, which prevented it entering the pelvis. As it was by this time dead, evisceration was performed, and the tumour, which proved later to be polycystic kidneys weighing 1 pound 9¼ ounces (g. 708), was evacuated, followed by birth of the child.

Following delivery the patient had a blood pressure of 200/125, and restlessness and twitching of the muscles. This subsided, and by the next day her blood pressure

was almost within normal limits. By the end of the first week, however, her blood pressure had gone up to 180/120 and remained at that level until the 4th week, when she finally ceased to attend. At this time the piperoxane test was found to be negative. The blood urea was 30 mg./100 ml. and a catheter specimen of urine showed no abnormality. The optic fundi were normal.

Foetal Post-mortem Report

General Appearances. The body was that of a female infant and its abdomen was opened in roughly the mid-line. The greater part of the intestine and liver had been removed, and was with the tumour which was received in a separate container. It appeared that the tumour had occupied the retroperitoneal tissues and there was possibly a septum dividing the two parts, but this could not be identified with any certainty. The aorta ran behind the mass. No renal arteries appeared to arise from the aorta, and no separate kidneys could be identified. The uterus appeared satisfactory. The tubes were greatly elongated over the lower part of the capsule of the tumour, which appeared to consist of the peritoneum covering the posterior abdominal wall. The left ovary was identified as a small nodule but the right could not be clearly found. A small nodule was present, which may have represented it.

Two doubtful ureteral openings were found in the bladder, but no ureter could be seen on either side.

The heart and great vessels appeared to be otherwise satisfactory, but the ductus arteriosus was still patent. The ribs on the right side of the chest had been fractured, and there was some bruising of the tissues on both sides of the thorax. The lungs had not expanded. The mouth and pharynx were not dissected. The skull contents were also not examined.

The Renal Tumour. This weighed 1 pound 9¼ ounces (708 g.). The appearances are those typical of a polycystic kidney.

(3) 1954. In February she was delivered of a stillborn macerated 32-weeks foetus without difficulty. During the antenatal period she had 4 attacks of pyelitis, always on the right side. At her first antenatal attendance, on the 14th week, her blood pressure was 120/80. There was no oedema, and no albuminuria. At the 18th week, her blood pressure was 176/110, and there was a trace of albumen in the urine. She refused to come into hospital, but promised to rest at home. Thereafter her blood pressure varied from 130/90 to 144/96, and there was albuminuria on several occasions. She had felt no foetal movements for one week before admission, and on admission in premature labour her blood pressure was 128/80. After delivery and in the puerperium it varied from 170/110 to 140/80, and, when she took her own discharge on the 12th day, it was 170/110. An intravenous pyelogram was taken on the 7th day of the puerperium. She declined to have it repeated.

Intravenous Pyelogram Report

The injection was terminated at 10 ml. owing to an intense venous spasm. There was no leakage at the site of the injection. The right kidney was excreting dye well, but the whole picture is so badly obscured by intestinal gas and bowel contents, as to render any opinion regarding the left kidney valueless. The bladder outlines normally.

Foetal Post-mortem Report

External Appearances. The body was that of a male foetus of about 32-weeks gestation. It was very macerated, and had obviously been dead for some time before delivery.

Internal Appearances. Head: The brain was too autolysed for any abnormality to be seen. *Chest:* No congenital anomalies were found in the heart and lungs. *Abdomen:* The abdomen was grossly distended. The kidneys were grossly enlarged and the cut surface was similar in appearance to sorbo rubber. The condition was very similar to the kidneys of the previous child. The remainder of the abdominal organs were too autolysed for critical examination, but no other obvious abnormalities were found.

History of Present Pregnancy

Despite her unfortunate obstetric history, the patient had persuaded her doctor to book her for confinement at home. Apparently the pregnancy was uneventful, being complicated only by mild hypertension in the later weeks. The first day of her last menstrual period was on the 23rd October, 1954, and her expected date of confinement the 30th July, 1955.

On the 3rd July, 1955, labour started at 10 p.m. and progressed rapidly. She was apparently fully dilated about 1 a.m. on the 4th July. Forceps were applied at the patient's home by her own doctor under open ether anaesthesia at 3.30 a.m. owing to delay in delivery. The head rotated from the right occipito-lateral position into the antero-posterior diameter and delivered. Thereafter delivery was found to be obstructed. After repeated attempts to extract the child by traction on the neck, the arms were drawn down. Delivery was still not found possible. By this time the child was obviously dead. The case was promptly sent to hospital. Morphine gr. ¼ (16 mg.) was administered at 4 a.m.

Condition on Admission on the 4th July, 1955 at 6 a.m.

The general appearances were those of a tired, frightened young woman of average nutrition. Her temperature was 98·4° F. (37° C.) and her pulse rate was 130 per minute. Her blood pressure was 170/120. From the vagina were protruding the head and arms of a foetus. The

foetus was obviously dead. There was much ecchymosis in the region of the mandible. The neck was attenuated, the cervical spine having been broken; it consisted only of soft tissues. The cardiovascular and respiratory systems showed no abnormality. On examination of the abdomen the height of the fundus was that of a full-time pregnancy. Regular uterine contractions of good quality were occurring every 5 minutes. Palpation revealed the back to be to the right. No foetal heart was heard. There were neither areas of tenderness nor guarding in the abdomen.

Vaginal Examination

The head and arms of the foetus lay outside the vagina as described. Under aseptic conditions a vaginal examination was performed with the patient in the lithotomy position. The vestibule was noted to be rather oedematous. Insertion of the hand into the uterus identified the back to be lying to the right, while the abdomen was grossly distended by a tumour of fairly firm consistency. The uterine wall appeared to be intact.

Procedure

The patient's general condition was considered sufficiently good for another attempt at extraction under general anaesthesia.

The patient's bladder was catheterized and 300 ml. of clear urine were evacuated. A pair of sharp-pointed scissors was inserted into the swollen abdomen a few inches distal to the xiphisternum. The abdominal wall was thus pierced, and the opening enlarged digitally. Attached to the posterior wall of the abdomen a tumour of rubbery consistency was palpated. Its size was not determined. It appeared to have a mid-line fissure and to arise from the pelvis of the child. Large portions of it were removed piecemeal, with difficulty, by the use of the fingers. Following this extraction of the foetus was accomplished easily by traction on the arms and the baby was thus delivered. The placenta was removed manually.

Foetal Post-mortem Report

External Appearances

The body was a full-time male infant. The abdomen had been opened. The liver and one kidney had been removed, and the head had been decapitated.

Internal Appearances

Cardiovascular System. The heart was normal in shape with hypertrophy of both ventricles. The valves and great vessels were normal. The pericardium and its contents were normal.

Respiratory System. There was no obstruction in the larynx or bronchi but both lungs were completely collapsed.

Alimentary System. The oesophagus, stomach, large and small intestines, were all normal. The pancreas, spleen, liver were all normal.

Central Nervous System. There was gross haemorrhage in the brain following the obstructed delivery.

Genito-urinary System. The kidneys were extremely enlarged and composed of multiple small cysts which were about the size of a pin head.

Each kidney measured 11 by 7 by 6 cm. and they weighed 2 pounds 1¾ ounces (958 g.) together.

Microscopic examination: The kidneys were composed entirely of cysts with areas of various sizes. The cysts were lined by a single layer of low cuboidal epithelium. In the larger cysts the epithelium became completely flattened. The wall of the cysts was loose connective tissue. Few leucocyte infiltrations were found in the stroma. Occasional small glomeruli were also present.

Puerperium. This was uneventful except for a slight rise in temperature.

On the fourth day, this rather wilful patient took her own discharge, declining absolutely to have any further investigations performed, either on herself or on any member of her family.

Discussion

In most obstetric textbooks polycystic disease of the kidney is cited along with ascites and urinary retention as a cause of enlargement of the foetal abdomen producing dystocia. Generally, however, the size of the kidneys is not such as to produce any real obstruction to labour.

Cases have been reported where renal hypertrophy has caused an obstruction to delivery, but such cases are rare.

We have traced only 2 reported cases in the literature of recent years. The first case was reported by Gonnet *et al.* (1937). The patient was aged 33, para-4, and at term delivered the head. The abdomen, however, was retained despite energetic traction. Evisceration was performed and delivery of a stillborn infant effected. Following delivery it was found that the vaginal vault had ruptured, but the patient recovered well. The foetal kidneys together weighed 1 pound 6 ounces (650 g.). In the second case, described by Clark and Gipson (1948), the obstetrician had considerable difficulty in delivering the abdomen because of its large size. The baby was, however, born alive, but died a few hours later. At post-mortem examination the kidneys were found to be enlarged by cysts of varying sizes and weighed together 1 pound 3 ounces (560 g.).

We have been unable to find in the literature a reported case of recurrent dystocia due to polycystic disease of the kidney.

Summary

(1) A case of obstructed labour due to enlarged polycystic kidneys causing gross enlargement of the foetal abdomen is described.

(2) The patient had a similar condition with two previous pregnancies. We have been unable to find a recorded case of recurrent obstruction of labour due to foetal polycystic kidney disease.

We wish to acknowledge our indebtedness to Mr. George Winchester, Consultant Obstetrician and Gynaecologist to the Hull Group of Hospitals, for his permission to publish this case, and to thank him for his encouragement and advice.

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CAESAREAN SECTION FOR FOETAL DISTRESS

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IT is only in the last 10 years that foetal distress has been accepted as an indication for Caesarean section. There are still those who consider such treatment as extremely radical (Editorial comment, *Obstetrical and Gynecological Survey*, 1955), and Louw (1955) thinks that it is an unsatisfactory indication because it can be so easily abused. Because of the controversy on the subject, we present a study of 130 cases in which Caesarean section was performed for foetal distress.

With the increasing safety of the operation there is a tendency towards its more frequent use. But how safe is it? In a series of 7,762 Caesarean sections collected from 19 British teaching hospitals for the years 1943–1947 by Marshall and Cox (1949) the maternal mortality was 0·99 per cent. Modern therapeutic methods have undoubtedly improved the position, and, in the United States, Harris *et al.* (1951) record 2,070 Caesarean sections with only 1 maternal death. De Soldenhoff and Brill (1954) report 500 sections without a death. Such results prove that section can be made almost as safe as vaginal delivery and justify the claim that the accepted indications for Caesarean section are too conservative. However, the fact is that there is still a slight maternal mortality from the operation which will vary more with the skill of the individual surgeon and the facilities at his disposal than with the indications for which he performs the operation.

Fitzgerald and McFarlane (1955) studied 206 cases of foetal distress and showed that active intervention as soon as the condition was recognized would prevent stillbirths. Walker (1954) advocates the serious consideration of section if foetal distress occurs, particularly in the case of the primigravida over the age of 25.

MATERIAL

One hundred and thirty consecutive cases in which Caesarean section was performed for foetal distress were selected from the records of three hospitals where we have worked.

	Cases
University College Hospital, London (1948–1952)	60
St. Thomas's Hospital, London (1950–1955)	31
Freedom Fields Hospital, Plymouth (1952–1954)	39

We have excluded cases of foetal distress associated with placental separation and prolapse of the cord, and there were only 5 cases of definite disproportion.

Whilst the criteria by which the distress was judged may not have been exactly the same, the indications were those usually accepted, namely, abnormality of the foetal heart rate or rhythm and meconium in the liquor. As De Soldenhoff and Brill (1954) state, these are signs that something has upset the foetal equilibrium so that, if labour lasts too long, there may be a fatal termination for the child.

Caesarean section was performed in all cases because the dilatation of the cervix was not sufficient to allow forceps delivery.

TYPES OF FOETAL DISTRESS

	No.	Deaths
Meconium and changes in the foetal heart	28	5
Meconium alone	52	3
Foetal heart rate below 110	21	0
Foetal heart above 160 ..	16	1
Foetal heart irregular ..	13	1
Total	130	10 (7·7 per cent)

In 52 of the cases there was meconium staining in the liquor alone. In 50 cases section was done because of changes in the foetal heart rate, whilst in 28 there were both meconium and changes in the heart rate. The presence of the two together was the most dangerous for the foetus, and in this group there were 5 deaths in 28 cases. Of these, 3 foetuses showed bradycardia, 1 had an irregular heart rate and the other had tachycardia. Eight of the 10 deaths were associated with the passage of meconium; in 1 the liquor was clear and in 1 the membranes were intact. Our observations are in agreement with Fitzgerald and McFarlane (1955) and Resnick (1955) that it is the "peasoup" meconium that is particularly dangerous. The slight green staining of the liquor has not the same serious significance.

AGE AND PARITY

There were 97 primigravid patients and 33 multiparous patients in the series. In the 97 primigravidae the age distribution was as follows:

	Total Cases	No. of Deaths
Below 25 years ..	24	1
25–34 years	55	7
35 years or more ..	18	1

Nine deaths occurred in the 97 primigravidae and 1 in the 33 multigravidae. It might, therefore, be reasonable to adopt a more conservative attitude towards operating on the latter group—in fact, to watch and wait in the hope that the patient may reach the second stage of labour, and it is in such cases that oxygen therapy may be particularly useful.

LENGTH OF LABOUR

It is difficult to reach any conclusions about the effect of the length of labour, since all cases were operated on during the first stage. However, we have no doubt that long labour predisposes to foetal distress, and few authorities would dispute this.

MATURITY

The outstanding feature of this study is the close association between foetal distress and postmaturity. Out of the 130 cases, in 58

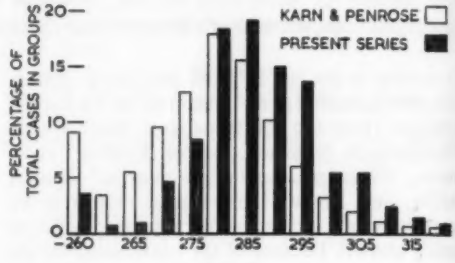

FIG. 1

Duration of pregnancy in days (including figures by kind permission of Professor L. S. Penrose).

(44·6 per cent) the gestation period was 290 days and over. The incidence of postmaturity found by Karn and Penrose (1951) in 13,730 deliveries is 24·5 per cent. There is a significantly greater incidence of postmaturity in our series ($p=0·0000001$).

The mortality rate in our Caesarean section cases was as follows:

	No.	Mortality	Mortality Per cent
Mature ..	72	1	1·4
Post-mature	58	9	17·3
Total ..	130	10	7·7

These figures emphasize the danger to the foetus which shows distress if the pregnancy is postmature ($p=0·003$).

HYPERTENSION

This is an important factor in the production of foetal distress, 60 cases (46·2 per cent) having a diastolic blood pressure of 90 mm. Hg or over at some time during pregnancy. To enable

comparison with Martin (1955) these figures have been corrected.

	Number of Cases	Hypertensive	Per cent
Martin (1955)	2,000	464	23·2
Present series	107	43	40·2

These figures are statistically significant (p=0·0001). If primigravidae after the 273 days of pregnancy are considered alone, 43 out of 87 (49·8 per cent) are hypertensive. If cases where artificial rupture of the membranes was carried out for hypertension are excluded, the incidence of hypertension in the remaining 89 cases is 37·1 per cent (33 cases).

Artificial Rupture of Membranes

This took place in 41 cases (31·5 per cent). The indications were hypertension, 18 cases, postmaturity, 8 cases, both, 9 cases, and others, 6 cases. It seems that the operation is associated with an increased incidence of distress. The incidence of hypertension is much greater amongst this group, being 65·9 per cent as opposed to 46·2 per cent in the whole group of cases, and this might account for some of the increase in distress, but not all of it.

Weight of the Foetus

This does not cause an increase in foetal distress in the primigravid patient until the foetus weighs more than 9½ pounds; 5 such foetuses suffered from distress. This is due either to relative disproportion or increased oxygen demand owing to excessive size of the foetus, or a diabetic tendency in the mother. It happens that all the foetuses of primigravidae weighing over 9½ pounds were postmature.

Discussion

In a series of 6,000 deliveries at University College Hospital (1948–1952), 1 per cent showed foetal distress for which Caesarean section was performed. It is therefore one of the commonest indications for operation.

Our results show that foetal distress is a problem in primigravidae and then only serious when associated with postmaturity. This is no new concept. It was shown by Barcroft and Young (1943) that there was a relative anoxia of the foetal rabbit in postmaturity, and Walker (1954) has published similar findings in the postmature human foetus. He showed the incidence of foetal distress to be low before the 40th week and to rise steadily with the degree of postmaturity, so that the obstetric death rate was three times as high at 43 weeks as at 40 weeks due to an increase in stillbirths. McKiddie (1949) has also emphasized the increased incidence of foetal distress in postmaturity, and the whole subject of prolongation of pregnancy has been exhaustively and excellently reviewed by Nesbitt (1955), who produces much evidence that the foetal environment deteriorates after term. Resnick (1955) studied foetal distress in 197 cases and assessed the foetal mortality in relation to meconium staining and postmaturity. Our findings confirm his, namely that the foetal mortality is highest when the liquor is thickly stained with meconium and when the foetus is postmature. Gibson (1955) has produced further convincing proof that postmaturity is responsible for a definite foetal mortality which results primarily from anoxia *in utero*, and this occurs mainly in the first and second stages of labour. The great quantity of literature on this subject all leads to the same conclusion—that postmaturity cannot be ignored.

The work of Dornhorst and Young (1952) suggests that foetal distress is due to some alteration in the mono-amine oxidase concentration in the placenta which prevents the inactivation of adrenaline and noradrenaline in the maternal blood. These authors have produced impairment of the placental circulation in the rabbit with the injection of adrenaline and noradrenaline into the maternal circulation, and it is possible that one of these two substances may be released in increased quantity in long labour and account for some cases of distress.

The question arises as to whether foetal distress of the dangerous type associated with postmaturity can be avoided by surgical induction of labour. Racker, Burgess and Manley (1953) take the extreme view that all patients should be induced who go past their expected date of delivery. Using Karn and Penrose's (1951) figures, this would mean inducing 58·1 per cent of patients for this indication alone. Undoubtedly surgical induction carries a mortality for the foetus

variously estimated at between 0·5 and 1·5 per cent (Martin, 1955). Martin has, therefore, suggested that only those cases with hypertension should be induced at term, the rest being allowed to go into spontaneous labour; but in all postmature labours repeated checking of the foetal heart is essential, and such labours should be conducted in a hospital where operative delivery can be immediately performed if indicated.

Hypertension does seem to be associated with the production of foetal distress in our series; although artificial rupture of the membranes predisposes to foetal distress as well, the operation does not account for the whole effect. Smyth (1956) agrees with the observation, but Fitzgerald and McFarlane (1955) could not find any association, possibly because they took too high a standard for hypertension (150/100 mm. Hg). Browne and Veall (1953) have demonstrated that hypertension, even if only of a mild degree, is associated with uterine ischaemia.

Some writers have pointed out the beneficial effect of giving the mother oxygen in cases of foetal distress. It is our practice to do so whilst preparing the patient for operation, and in many instances the foetal heart becomes more normal. This effect, however, may be temporary, for which reason we do not give oxygen until a definite decision has been reached as to whether Caesarean section is to be carried out or not.

Conclusions

(1) Foetal distress of sufficient severity to require consideration of Caesarean section occurs in about 1 per cent of maternity hospital admissions.

(2) Foetal distress is not a problem of significance in prematurity and infrequently occurs before the 270th day of pregnancy.

(3) The serious problem is found in postmature primigravidae. These should be treated by immediate operative delivery and on no account should there be delay.

(4) In the case that is not postmature which develops foetal distress, it may be possible to avoid section in some instances where full dilatation may be soon anticipated and where the patient is in other respects normal.

(5) As multiparae tend to have quick labours, this group may also be allowed to progress with their labours where an early termination of the first stage seems probable.

(6) Hypertension is an important factor in the aeticlogy of foetal distress. Cases with hypertension should not be allowed to become postmature. If they do, surgical induction is indicated.

(7) The routine surgical induction of labour in all women at term is deprecated as the operation itself is associated with a foetal mortality.

(8) Oxygen should be administered to all cases with foetal distress once a decision has been made as to whether Caesarean section is indicated or not.

Acknowledgments

We are indebted to the consulting staff of the Obstetric Departments at St. Thomas's and University College Hospitals, and also Mr. A. Concanon of Plymouth, for permission to use records of their cases. In addition we are very grateful to Dr. W. J. Martin of the Statistical Research Unit, London School of Hygiene and Tropical Medicine, for the statistical data.

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PAGET'S DISEASE OF THE VULVA

BY

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IN almost all the previously reported cases of extra-mammary Paget's disease, discussion has centred around the true nature of the "Paget cell". Weiner (1937) and Huber, Gardiner and Michael (1951) are of the opinion that the skin lesion is secondary to a carcinoma of apocrine glands and the Paget cells metastatic tumour cells. There are other authorities however who oppose this view (Willis, 1948; Jeffcoate, Davie and Harrison, 1944). Jeffcoate and his colleagues would confine the term Paget's disease to the lesion of the breast and they maintain that the vulval lesion is the result of a primary epidermal change which may be either precancerous or cancerous. The most recent work by Lennox and Pearse (1954) and Paget, Rowley and Woodcock (1954) has, by the use of histochemical methods, produced very strong evidence in support of the metastatic theory, and in the case reported here we are able to confirm these findings. Moreover, a primary adenocarcinoma of probable sweat gland origin has been demonstrated.

The treatment in most cases appears to have been based on the assumption that the condition is a primary epidermal change of, at the worst, low malignancy. The present case and its subsequent history reveals the fallacy of this premise.

CASE REPORT

Mrs. I.L., aged 67 years, para-3, housewife, had for 2 or 3 years experienced constant irritation of the right side of the vulva. Self treatment had been carried out by the local application of various ointments and lotions, but without relief. For some 3 months the condition had become painful and medical advice was sought.

Previous History. Subtotal hysterectomy had been performed 20 years ago followed by an appendicectomy 1 year later.

General Examination. Some arthritis of the lower spine and right hip joint was present, but apart from this no general medical disability existed.

Local Examination. The vulva presented a reddened, mottled, eczematoid appearance covered by numerous white macerated patches and scabs (Fig. 1). There was swelling of both labia extending from just below the mons veneris to the perianal region. The surface showed evidence of scratching but no ulcer was present. The swollen red labia were generally indurated but palpation failed to reveal any localized tumour. There was neither excessive shrinkage of the introitus nor vaginitis present. Fungus infection was excluded.

On the right side no enlarged inguinal lymph nodes were palpable, but on the left some doubtful subinguinal nodes were to be felt.

Examination of the urine revealed no abnormal constituents, and a blood sugar curve was within normal limits.

Initial treatment mainly along hygienic lines had but little and temporary effect, and in October, 1954, local vulvectomy was performed. Healing was by primary union and all symptoms were relieved, but following the histological diagnosis of Paget's disease of the vulva with an underlying carcinoma, further operative measures were pressed. In January, 1955, extensive bilateral inguinal lymphadenectomy, together with excision of a further portion of apparently affected perineal skin, was carried out. The left subinguinal nodes, together with the lymph node of Cloquet were clinically involved. Neither the right inguinal nodes nor the external iliac nodes on either side appeared to be affected. Healing was slow but ultimately satisfactory.

In June, 1955, the patient was re-admitted with clinical evidence of carcinomatosis and died on the 29th June, 1955.

Pathology

Macroscopic

The original specimen (October, 1954) consisted of the vulva and underlying fatty tissue. The right labium majus was diffusely enlarged and oedematous, and in the fixed specimen the skin over it had a mottled granular appearance, with small, raised, firm, irregular white areas. This surface granularity extended on to the anterior portion of the right labium minus and prepuce, and on to the mons veneris in the area adjacent to the prepuce. The left labium majus was of normal size, but granularity of the skin could be seen on the medial aspect of the anterior portion. The rest of the vulva showed no macroscopic abnormality. Beneath the mucosa in the fold between the right labium majus and the prepuce, at the level of the upper limit of the prepuce, a small discrete nodular tumour was found. This measured 6×6 mm., and was clearly separated from the overlying epithelium. Macroscopically the tumour appeared to be encapsulated.

The material from the second operation (January, 1955) was as follows: Left inguinal nodes—a mass of fibro-fatty tissue 10×4×4 cm., containing 3 grossly enlarged lymph nodes and several small ones. The large lymph nodes were all obviously infiltrated by tumour.

Right inguinal nodes—fibro-fatty tissue containing 6 lymph nodes, none of which appeared to be infiltrated by tumour.

Microscopic

All sections of the vulva show similar changes. The striking feature is the presence of large clear Paget's cells in the juxta-basal layer of the squamous epithelium, occurring both singly and in groups, and in many places distending the tips of the rete pegs (Fig. 2). Single cells have been carried into the Malpighian layer and even into the keratin layer. They are also present in the outer layers of the epithelium of hair follicles and many sweat gland ducts and acini are distended and distorted by the presence of Paget's cells between the myo-epithelial cells and the glandular epithelium (Fig. 3). The squamous epithelium varies in thickness and appearance from place to place. In some areas there is little keratin and the Malpighian layer is reduced to one or two cells in thickness; in others there is gross hyperkeratosis and acanthosis. Small areas of ulceration are frequent. The dermis shows a dense round cell infiltration. Towards the periphery of the lesion, the epidermal changes are reduced to a minimum and the tumour cell infiltration is patchy.

Sections of the small nodular tumour mass show a pseudo-capsule produced by condensation of the surrounding fibrous tissue (Fig. 4). At one point in this dense fibrous tissue, intact normal sweat gland acini can be seen. Multiple sections failed to reveal any direct connexion between the tumour and the overlying skin. The tumour itself is composed of small and large groups of polygonal cells which have vesicular nuclei and frequently show vacuolated cytoplasm (Fig. 5). Many of the cells are surrounded by basophilic material which is P.A.S. positive and histologically resembles mucin (Fig. 5). Some of the larger groups appear to be distending a lumen which is bounded by a basement membrane, and between the basement membrane and the tumour cells a single layer of flat cells resembling myo-epithelial cells can be seen (Fig. 5). In one of the dense bands of fibrous tissue passing between the groups of tumour cells there is a normal sweat gland acinus. Sections of the right inguinal lymph nodes show no evidence of tumour; those from the left are extensively infiltrated by tumour cells.

Sections of the tumour deposits found at post-mortem show a similar structure to those seen in the invaded lymph nodes.

Histochemistry

Many of the characteristic Paget's cells in the epidermis give a positive periodic acid Schiff reaction, as do many of the tumour cells in the lymph nodes and in the discrete tumour mass. That this positive reaction is due to the presence of mucin has been confirmed by the Alcean blue stain, mucicarmine and persistence of the positive P.A.S. reaction after diastase treatment. The P.A.S. positive material shows no metachromasia when stained with toluidin blue. Best's stain for glycogen is negative as is sudan black B.

FIG. 1
Paget's Disease of the Vulva.

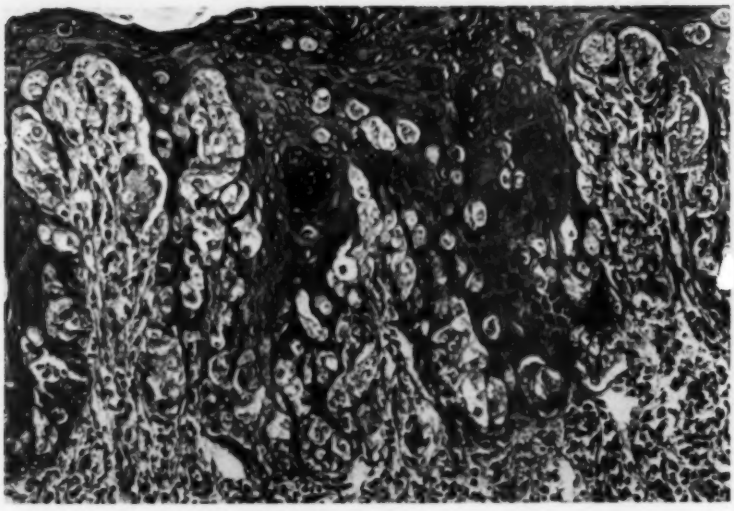

FIG. 2
The epidermal lesion. ×180.

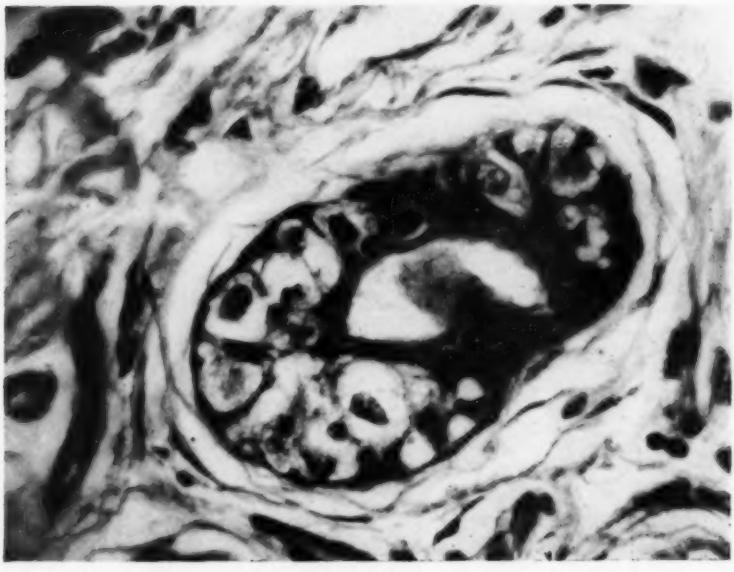

FIG. 3
Paget cells between the myo-epithelial cells and secretory epithelial cells of a sweat gland acinus. ×675.

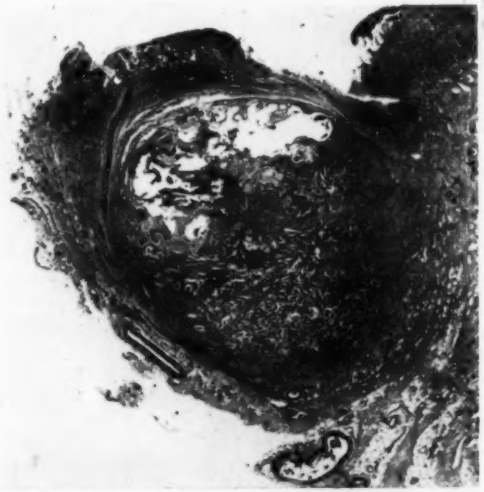

FIG. 4
Lower power view of the primary tumour mass. ×10.

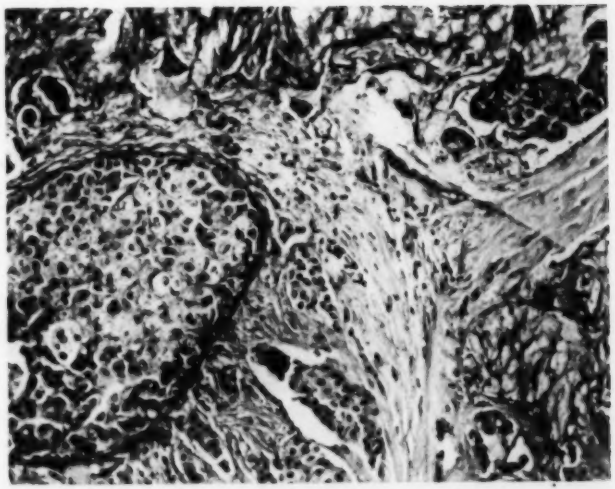

FIG. 5
Portion of the primary tumour. ×160.

Post-mortem Examination

At post-mortem the operation site was seen to be healed and healthy. The following report is a brief account of the relevant findings:

Abdomen. There was a diffuse mass of tumour tissue in the left inguinal region and extending along the left wall of the false pelvis. The femoral vein passed through the centre of this mass. All the para-aortic lymph nodes were enlarged and infiltrated by tumour, this being most marked on the left side where the para-aortic lymph nodes were continuous with a chain of invaded lymph nodes following the line of the left femoral vein and external iliac vein.

The left kidney showed early hydronephrosis and hydro-ureter. There were no tumour deposits present.

The ovaries were atrophic. There was no evidence of tumour. The vaginal surface of the cervix was white and a little indurated, but there was no evidence of tumour.

The bulk of the liver tissue had been replaced by tumour tissue, which was present as small nodules and confluent masses.

Thorax. There were small nodules of tumour tissue scattered diffusely throughout both lungs and all the tracheo-bronchial and mediastinal lymph nodes were enlarged and obviously infiltrated by tumour.

The other organs were normal. No primary tumour was found.

Sections of the tumour deposits showed a similar structure to that seen in the deposits of the lymph nodes.

Discussion

In our opinion the histological and histochemical findings in this case indicate that the primary tumour present in the vulva is a sweat gland carcinoma and give support to the metastatic theory of the origin of the Paget's cells.

The appearances and staining reaction of the discrete tumour mass are those of an undifferentiated mucin-producing adenocarcinoma. The small size, the situation, and the histological appearances suggest that it is of sweat gland origin, and Lennox and Pearse (1954) state that the presence of mucin in any quantity in a skin tumour is an almost invariable sign of sweat gland origin. The only other possibility is a metastatic deposit from an adenocarcinoma elsewhere. Although this at first could not positively be excluded, there was never any clinical evidence of another primary tumour, and post-mortem examination failed to reveal anything other than multiple secondary deposits from a mucin-producing adenocarcinoma.

Lennox and Pearse (1954) give histochemical proof of the presence of mucin in Paget's cells, and for this reason state that Paget cells are not epidermal in origin. We agree with this statement and believe the presence of mucin in both the Paget cells and the primary tumour shows that they have a common origin. It is significant here to recall Paget's original suggestion that the condition he had described in the skin of the breast would be found in other parts of the body in association with an underlying carcinoma.

Muir (1927) propounded the theory that infiltration of squamous epithelium by tumour cells, as seen in a typical Paget's disease of the breast, may only occur when the epithelium from which the tumour is arising is in direct continuity with the squamous epithelium affected. If this theory is accepted for extramammary Paget's disease, the presence of Paget's cells in the squamous epithelium in this specimen can be considered evidence in favour of the sweat gland origin of the primary tumour.

Biopsy is necessary for diagnosis, since macroscopic appearances may be confused with other diffuse skin conditions of the vulva. It must also be realized that skin infiltration may extend beyond the limits of clinical involvement. Even microscopically the epithelium may be normal except for the presence of occasional Paget's cells.

The malignant character of this condition is clearly demonstrated. The extensive secondary deposits in the inguinal lymph nodes and the eventual death of the patient from carcinomatosis serve as a reminder that this disease should be treated as radically as any other malignant condition of the vulva.

SUMMARY

(1) A case of Paget's disease of the vulva with an underlying adenocarcinoma of sweat gland origin is described.

(2) Histological and histochemical evidence of the relationship of the two conditions is given.

(3) It is suggested that biopsies of such vulval lesions should always be taken and in a proved case radical surgery be undertaken.

We would like to express our thanks to Dr. Hamilton-Paterson for his help, particularly in the preparation of the photomicrographs.

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FIG. 1
The symphysis pubis joint of the mother.

FIG. 2
The symphysis pubis joint of the mother, whilst standing on one leg.

FIG. 3

The symphysis pubis joint of the daughter on the sixth day after delivery.

HEREDITARY PELVIC ARTHROPATHY OF PREGNANCY

BY

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IN the comprehensive study of Pelvic Arthropathy of Pregnancy published in this *Journal* by Young (1940) there is no reference to heredity in the discussion of the aetiology.

The unusual coincidence of Pelvic Arthropathy in an 18-year-old primigravida whose mother developed this condition during her fifth pregnancy in 1953 appears worthy of publication.

The mother (M.D.), aged 42 years, complained in the sixth month of her fifth gestation of severe backache, which was of recent and insidious onset: she had not experienced any such discomfort during the previous pregnancies. Examination revealed marked tenderness over both sacro-iliac joints and the symphysis pubis. X-ray investigation showed considerable relaxation of the pelvic joints, especially the symphysis pubis (Figs. 1 and 2). The patient obtained great relief by rest in bed, with fracture boards under the mattress in the antenatal ward, and in this way was able to enjoy reasonable comfort until she delivered herself spontaneously at term. The symptoms then slowly disappeared. In 1955, she re-appeared at the Antenatal Clinic in early pregnancy, and, although the same symptoms were again beginning to worry her, the fitting of a good supporting corset enabled her to continue to live a semi-active life at home until delivery. During the gestation, this patient brought with her to the Antenatal Clinic her 18-year-old daughter (M.S.), who was also pregnant.

This young woman showed no signs of inheriting her mother's symptoms. When she was in labour, however, the tenderness over the symphysis pubis was so marked, that efforts to palpate the presenting foetal head per abdomen had to be abandoned. The patient seemed rather embarrassed over this tenderness and endeavoured to explain that it was due to a fall 3 weeks previously: she had a normal spontaneous delivery. On the sixth day post-partum, an X-ray investigation of the symphysis pubis revealed marked separation at this joint (Fig. 3), and the tenderness persisted. When she was re-examined 6 weeks later, all traces of tenderness had disappeared. She at no time complained of any tenderness over the sacro-iliac joints.

In his detailed description of Pelvic Arthropathy of Pregnancy, Young stated that some of his cases had dated their symptoms from an accident. The hereditary factor was then unknown: these two cases, which suggest that a hereditary factor may exist, are therefore reported.

I wish to express my thanks to Dr. M. A. Fitz-Gerald for permission to publish his X-ray plates.

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SPREAD TO SKIN FROM CANCER OF THE CERVIX UTERI

Report of a Case

BY

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IN the literature only 3 cases of metastasis to the skin in carcinoma of the cervix can be found. Marcial-Rojas and Meigs (1955) reviewed 169 cases of cancer of the cervix uteri and reported 1 case of skin involvement (Meigs, 1956, has seen 1 further case). Friedl (1934) reviewed the German literature and here one finds a case described by Virchow (1855) and 1 by Foerster (1858). More recently a Russian paper (Mandel'shtam, 1953) mentions skin metastases. Graves, Kickham and Nathanson (1936), Behney (1933) and Shields Warren (1931) have investigated large series of cases of cancer of the cervix noting all secondary deposits and in none were the skin tissues involved.

The following is a case report in which the skin of the abdominal wall and thighs was infiltrated by diffuse secondary deposits.

CASE REPORT

P.H., aged 34 years, was admitted to another hospital on 23rd January, 1955 for investigation of post-coital bleeding of 4-months duration. Her previous menstrual history was normal and her obstetric history was that of a breech twin delivery in 1950 (cervical laceration was not recorded). A diagnosis of a squamous celled carcinoma of the cervix was made and as this was in the clinical group of Stage IV of the League of Nations classification radium was the treatment of choice. Three courses of radium application totalling 7,260 mg./hours were given, on 25th February, 1955, 5th March, 1955 and 18th March, 1955.

She was discharged from hospital on 26th March, 1955, but was admitted to this hospital on the 15th October, 1955 in a terminal stage of carcinoma of the cervix with impairment of kidney function, anaemia, and "oedema" of the anterior abdominal wall and thighs. This "oedema" was noted by one of us (M.S.) as having the appearance of "carcinoma en cuirasse". The patient died on 20th January, 1956.

AUTOPSY FINDINGS

An autopsy was performed 6 hours after death.

External Appearance. The body was that of a young female subject showing oedematous swelling of anterior abdominal wall and thighs. The skin surface gave the appearance of that described as "peau d'orange".

Thorax. No gross abnormality in lungs or heart. No secondary deposits present.

Abdomen. On opening into the abdominal cavity it was noted that the anterior abdominal wall below the umbilicus was very firm and indurated and that the skin and subcutaneous tissues were infiltrated by white fibrous-like strands. A similar appearance was found in the superficial tissues of both thighs. The pelvic tissues were fixed in a mass of secondary growth extending bilaterally to the bony wall of the

FIG. 1

Section of abdominal wall showing invasion of cutis vera. ×160.

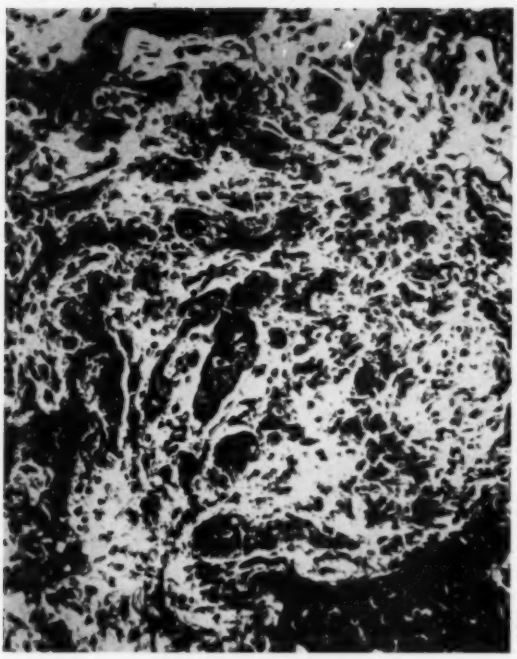

FIG. 2

Section of skin from right thigh showing groups of malignant cells in cutis vera. ×170.

pelvis. The para-aortic lymph glands, the peri-ureteric pathway and perinephric tissues were solid with secondary growth and in the midst of the latter were the grossly hydronephrotic kidneys. The uterus showed diffuse secondary involvement of the myometrium; the area occupied by the cervix had sloughed.

Pieces were taken for section from the abdominal wall, uterus, abdominal lymph glands and thighs. Histological examination of the abdominal wall and the superficial tissues of the thighs shows invasion of the cutis vera (Figs. 1 and 2) by squamous cell carcinomatous deposits similar to those found in the glands and in the original biopsy of the cervix.

Summary

A case of carcinoma of the cervix uteri is reported with metastases into the superficial tissues of the abdominal wall and thighs. This is apparently a rare extension as only 3 previous cases are reported in the literature. One might, however, postulate that this type of extension sometimes has been missed and mistaken for oedematous swelling as indeed it was described by several observers of this case.

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ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

At the Meeting of Council held in the College House on Saturday, 26th January, 1957, with the President, Sir Charles Read, in the Chair, the following were elected to **Membership of the College:**

Douglas Crowe Aird.
George Bryan Batchelor.
Ralph Anthony Timothy Boland.
Graeme Dickinson Desmond Cable.
Mahomed Ismail Cassimjee.
John Samuel William Chambers.
Probhat Kumar Choudhuri.
Charles Alan Blake Clemetson.
Kenneth Ivor Digwood.
Ammud Freier.
William John Garrett.
William Gault.
William Gavin.
Ivan Goldman.
Christoffel Jacobus Goosen.
Bernard Kirsch.
Margaret Amy Lakeman.
Edwin William Lillie.
Hamish Heathcote McCrostie.
John George Markus.
Andrew Edward Bertie Matthews.
Terence Thomas Erskine Michael.
Antony Bruce Miller.
Arun Kumar Mitra.
Jessie Mary Buchanan Muirhead.
Albert Gunaratnam Muttuthamby.
Anthony Brian Lowsley Peake.
Allan Clarke Cullen Pinion.
Lawrence John Rice.
Ray Richards.
Thomas Joseph Ryan.
Grahame Julian Witherington Stump.
Sarosh Meher Thanevala.
Kenneth Francis Gilmore Wilson.
Robert Yule.

Sir Russell Brain, Bart., P.R.C.P., and Doctor I. C. Rubin of New York, have been elected to the Honorary Fellowship of the Royal College of Obstetricians and Gynaecologists in recognition of their outstanding services to medicine.

REQUESTS FOR BACK ISSUES OF THE JOURNAL

Requests for complete sets of the back volumes of the Journal are occasionally received. The Secretary of the College would be glad to receive offers of back sets.

The following complete volumes are held in stock: Vols. 56 (1949), 58 (1951), 59 (1952) and 62 (1955).

In addition the following back numbers are in stock: Vol. 53 (1946), Nos. 3, 5 and 6; Vol. 54 (1947), Nos. 5 and 6; Vol. 55 (1948), Nos. 4, 5 and 6; Vol. 60 (1953), Nos. 3, 4 and 5; Vol. 61 (1954), Nos. 1, 5 and 6.

HOSPITAL REPORTS

BY

J. S. TOMKINSON, M.B., F.R.C.S., M.R.C.O.G.

THE CLINICAL REPORT OF THE MATERNITY HOSPITAL, CAMBRIDGE, FOR 1953

THIS is the first report published by this hospital and in the Survey details are given of the history of the hospital. The report follows the recommendations of the Royal College of Obstetricians and Gynaecologists with minor alterations. During the year, 1,759 deliveries occurred, of which 226 were non-booked (13·6 per cent). The 100 beds available were split up into 24 antenatal, 64 lying-in, 4 isolation, with 8 in the premature baby unit. No maternal death occurred; there was a stillbirth rate of 35 and a neonatal death rate of 17·8. An additional table is included of the foetal mortality in various conditions and operations; also one indicating the various types of anaesthesia and analgesia used.

Three cases of special interest are mentioned.

(1) A ruptured uterus following classical Caesarean section, (2) a septate uterus and vagina, and (3) an atypical case of concealed accidental haemorrhage of the Couvelaire type but without pain, real tenderness and hardening of the uterus: a laparotomy was performed, the foetus delivered by section and a subtotal hysterectomy carried out as the uterus failed to contract. The uterus of the last case is in the museum of the Royal College of Obstetricians and Gynaecologists.

The respective rates for forceps deliveries and Caesarean sections were 7·5 per cent and 3·4 per cent. In 7 cases a classical route was used, followed once by sterilization and thrice by hysterectomy (for fibroids in an elderly primigravida with quiescent tuberculosis, for the Couvelaire uterus, and for beginning rupture of the uterus in a case with a fibroid obstructing labour).

This has been an interesting report to peruse and it is an account of a successful year's endeavour.

CLINICAL REPORT OF THE MATERNITY DEPARTMENT OF THE PADDINGTON GENERAL HOSPITAL FOR 1954

THIS department consists of 75 lying-in, 15 antenatal, 11 labour ward beds and a premature baby unit of 8 cots. The majority of cases are booked on obstetric, medical or social grounds. A change in diet has been made for patients in labour, aimed at lessening inhalation complications of anaesthesia and also of ketosis. Two-hourly meals are given, rich in carbohydrate, readily absorbed, and easily aspirated through a Ryle's tube.

The report follows the recommendations of the Standard Report Committee of the Royal College of Obstetricians and Gynaecologists. A total of 2,149 patients were delivered, with 2 maternal deaths, a stillbirth rate of 17·4 and a neonatal death rate of 17·7. One maternal death occurred in a patient, aged 32, of cardiac failure due to rheumatic mitral stenosis; failure had occurred in a previous pregnancy, after which she refused sterilization. During the present pregnancy she once discharged herself from hospital and on more than one occasion did not keep her hospital appointment. Eventually she collapsed at home and was dead on arrival at hospital. The second death occurred from multiple haemorrhages, six weeks after delivery, due to acute myeloid leukaemia.

Cases of special interest mentioned are those of:

(1) Septic stomatitis as a result of regurgitation of gastric contents during second stage of labour.

(2) Extra membranous pregnancy (the patient losing liquor from the 26th week of amenorrhoea until she delivered herself at the 38th week of a baby with joint deformities and weighing 3 pounds 13 ounces).

(3) Vesico-vaginal fistula following spontaneous delivery (successfully repaired).

(4) Bilateral cerebellar tuberculoma occurring in pregnancy.

The forceps rate was 5·6 per cent; the use of "trial of forceps" in the operating theatre was used in a small number of selected cases of disproportion. Caesarean section was performed in 87 cases (6 classical sections) an incidence of 4·05 per cent. Post-partum haemorrhage occurred in 4·8 per cent and a manual removal of the placenta in 1·2 per cent; of the 26 patients in whom the procedure was carried out, morbidity occurred in 6.

The department is to be congratulated on a most successful year's work, the busiest since 1950 when their first report was published.

THE MATERNITY REPORT OF KING'S COLLEGE HOSPITAL FOR 1954

THIS concise report follows the recommendations of the Standard Report Committee of the Royal College of Obstetricians and Gynaecologists. It is well known that this department of King's College Hospital deals with an abnormally large number of diabetic women; its policy and practice may be obtained from the writings of the staff. No mention is made of the beds available to the unit, but a total of 784 deliveries were carried out during 1954, made up almost equally of primiparae and multiparae. Two maternal deaths occurred, from eclampsia and pulmonary embolus.

Thirty-two cases of diabetes were delivered in the hospital (12 by lower segment Caesarean section). The overall forceps rate was 18·6 per cent and the Caesarean section rate 7·8 per cent. The stillbirth and neonatal death rates were 28 and 27·7 per thousand respectively.

BOOK REVIEWS

"Disease in Infancy and Childhood." By RICHARD W. B. ELLIS. 2nd Edition. Pp. vii+710, with 333 illustrations. E. & S. Livingstone Ltd., Edinburgh. 1956. Price 50*s*.

THIS is the second edition of a highly successful textbook on paediatrics by the Professor of Child Life and Health in Edinburgh University. It provides a most stimulating introduction to the whole subject of disease in childhood.

The arrangement is unusual but effective, the diseases being grouped according to the ages involved or the type of aetiology rather than in the customary systemic classification. Thus there is a large section devoted to neonatal disorders and chapters on congenital malformations, neoplastic disease, allergic disorders, tuberculosis, etc.

Two chapters are concerned with the influence on health of constitutional factors (age, heredity, immunity, etc.) and of social and economic factors (illegitimacy, employment of mothers, overcrowding, war, etc.); the latter in particular is most valuable and interesting.

In the opening chapter it is pleasing to find at long last an English textbook which gives not only the means, but also the standard deviation of the means of measurements in childhood—and explains their use! It is also satisfactory to find prominence given to the commoner diseases of childhood, colds, colic, acute infections, fevers, etc., in addition to adequate representation of rarer illnesses.

The book is well written and beautifully produced; it is illustrated by over 300 photographs, many in colour, which are not merely decorative but enhance the value of the text.

Medical textbooks are sometimes criticized on the score of imbalance in the subject matter. This book could be cited as an example; for instance fourteen pages are devoted to an obsolescent disease, congenital syphilis, and only six to the ever-flourishing fits and convulsions. It is also frequently said that with the growth of medical science the day of the one-man medical textbook is past. In the reviewer's opinion, however, the one-man textbook can only survive if the reader is prepared to tolerate and even welcome unevenness of presentation. In attempting to cover all their subjects authors usually lose more in authority than they gain in comprehensiveness. In this book, for the most part so obviously the work of an expert, there is, for instance, a small section on genetics which is muddled and in places misleading.

In his election manifesto to the University of Oxford Sir Alan Herbert wrote—between extensive reviews of Divorce and Foreign Affairs—"Agriculture: I know nothing of agriculture." This approach could be warmly recommended to medical authors. It is after all valuable to know not only what are his especial interests, but also what information a clinician of great eminence has been able to do without in his career. All that is necessary is that he should refer the reader to the authority he has found most useful.

However, this is a minor criticism, and one which applies less to this textbook than most. In the reviewer's opinion this is easily the best paediatric textbook of single authorship in the English language. It can be strongly recommended.

"Williams' Obstetrics." By NICHOLSON J. EASTMAN. 11th Edition. Pp. x+1212. Many figures, some in colour. Appleton-Century-Crofts, Inc., New York. 1956. Price 105*s*.

THE appearance of a new edition of *Williams' Obstetrics* is an event in obstetric literature. This, the eleventh edition, as was the tenth, is edited by Professor Nicholson J. Eastman.

Thanks to the founder author this book throughout its career has been characterized by the emphasis which it places on "cultural" values. In this edition this aim is continued and it is well exemplified in the 240 pages (about one-fifth of the total volume) devoted to anatomy and physiology. These chapters have been well brought up to date and in their style, content and illustrations maintain the high standard set by J. Whitridge Williams.

Many sections have been completely rewritten and a new chapter on Psychiatric Aspects of Pregnancy and Childbirth has been added. In this chapter Dr. Leo Kauner discusses the emotional attitudes of the mother to her pregnancy, her labour and her child. He indicates that in his intimate and privileged relation to the family the obstetrician is "in a strategic position to function as the ideal mental hygienist of pregnancy and childbirth". It was found that, "unless there are physical obstacles, breast feeding makes for a happier contact between mother and child than bottle feeding" and "it has been established that occasional picking up and fondling, far from resulting in the dreaded spoiling, builds in the child a sense of security and of being accepted and loved".

The long chapter on the Toxaemias of Pregnancy has been reviewed critically by Dr. Leon C. Chesley, the well-known worker in this field. A comparison with older editions of the book reveals the extent to which the attitudes of the clinician and pathologist have shifted. "Low Reserve Kidney" and "Nephritic Toxaemia", which occupied such a large place, have disappeared. It is claimed that "the uterine ischemia theory of eclampsia (first advanced in clear-cut fashion in 1914 by James Young and subsequently sponsored, in one connexion or another, by Beker of Holland, Dexter and Weiss, Ernest W. Page, Dieckmann and many other authorities) . . . is probably more widely held today than any other explanation because it fits in well with many known facts about eclampsia".

For severe post-partum haemorrhage resistant to oxytocics preference is given to the "British method" of bimanual compression and substantial quotations from *The Abnormal in Obstetrics* by Berkeley, Bonney and MacLeod and from *Midwifery by Ten Teachers* are given in support of this method as against the "American method" of uterine packing.

This is a book which can be recommended without qualification to those of all grades of obstetric experience —student, practitioner and consultant. We have already alluded to the high standard of the illustrations. In other respects, also—paper, printing and binding—the editor and publishers are to be congratulated.

"Before and After Childbirth." By JANE MADDERS, M.C.S.P., Dip.Phys.Ed. Pp. 31. Illustrated. E. & S. Livingstone, Ltd., Edinburgh and London. 1955. Price 3*s*.

THIS small volume is one of the valuable series published by Messrs. E. & S. Livingstone for the use of mothers before and after the birth of the baby. With the aid of excellent photographic illustrations it describes the exercises suitable for the antenatal and postnatal periods and for the "relaxation" that now in many clinics constitutes an important preparation for childbearing. The descriptions are so simple and the illustrations so well chosen and so clear that the various procedures can be easily followed by the mother herself. At the same time it would have been well if the author had issued a warning that in a certain proportion of women there is excessive softening and mobility of the pelvic joints during pregnancy and that in these patients the exercises may cause damage to the ligaments and joints. The occurrence of pain on exercising indicates the need for the patient to consult her doctor.

"Gynecological Cancer." By JAMES A. CORSCADEN, M.D. 2nd Edition. Pp. x+546, with 116 figures and photomicrographs. Baillière, Tindall & Cox, London. 1956. Price £4.

THE second edition of Dr. Corscaden's excellent book on malignant disease in the female genital tract, published five years after the first edition, has been well revised and greatly extended. It is now brought up to date including recent advances in therapy and gives a complete survey of our present knowledge of the cancer problem in gynaecology. The list of references following each chapter has been amplified and contains all recent publications of note.

The fact, however, that the *leitmotif* of the first edition: "Diagnose early, the over all cure rate can be raised from 20 per cent to 80 per cent, if the diagnosis is made in time", continues to be the *leitmotif* of the second edition, throws a sad light on the slow progress of cancer consciousness. The author quotes Howson and Montgomery in the Philadelphia Committee Report: "Delay in diagnosis was the physician's fault in 27 per cent of cases, averaging 7·4 months for cancer of the cervix, 13·7 months for cancer of the uterine body, 9·6 months for cancer of the ovary and 19 months for cancer of the vulva." In nearly half the cases (49·3 per cent) the cause of the delay in diagnosis was failure to examine. The emphasis Dr. Corscaden lays on early diagnosis and the fervour with which he advocates routine gynaecological examinations are well understood when we read these striking figures.

The structure of the book has not changed but its volume has been greatly increased. Malignancy of each female genital organ is discussed in a separate chapter, all of which have been revised and amplified. The chapter on ovarian carcinoma has been almost completely rewritten, but one still regrets the scarcity of illustrations compared with the rich material of other sections of the book and the brevity with which the treatment of ovarian malignancies is dealt with. Compared with the complete discussion of surgical, radiotherapeutical and combined therapy of cervical cancer, one feels that ovarian carcinoma has been treated like a stepchild. This is the more regrettable as the prognosis of ovarian cancer is so infinitely worse than in other genital malignancies.

One also regrets that Dr. Corscaden has omitted to show cytological and colposcopic photomicrographs. Although he stresses the importance of early diagnosis and the importance of the Papanicolaou smear technique, there is not a single illustration of exfoliated cells.

Notwithstanding these few minor criticisms, Dr. Corscaden's book is a standard work on gynaecological cancer and the second edition deserves the same enthusiastic reception in specialist as well as in student circles that was given to the first edition.

E. Wachtel

"They Did Not Pass By—The Story of the Early Pioneers of Nursing." By DENIS G. MURPHY. Pp. xii+208. Longmans, Green and Co., London, 1956. Price 10*s*. 6*d*.

EVEN in these modern times there is much to be gained from a study of the ancients in almost every sphere of human activity. Nowhere is this more profitable than in regard to the nursing profession. In this masterly narrative the Reverend Denis G. Murphy illustrates vividly how modern nursing methods of practice and organization were successfully employed by the devoted and devout members of the Religious Orders between the dawn of the Christian era and the establishment of modern nursing by Florence Nightingale and her associates during the last century.

As might be expected the emphasis is on the contribution of the Roman Catholic Church and it comes as something of a surprise to find that even Miss Nightingale herself was at one time a prospective convert.

This book will make entertaining reading for all who are interested in the history of nursing or of the Roman Catholic Church.

"Natural Childbirth." By H. B. ATLEE, M.D., F.R.C.S., F.I.C.S. Pp. v+79, with 7 illustrations. Blackwell Scientific Publications, Oxford, 1956. Price 21*s*.

THIS wafer thin volume of the American Lecture Series is intended to present the teaching and philosophies of Grantly Dick Read in a presentable form to women during pregnancy, as a preparation for labour. Even the

author is somewhat at a loss to define "Natural Childbirth". Ignoring the many slang expressions used, and the doubtful scientific basis of the effective mechanism, there are described some useful points on how to replace fear by faith, and distressing pain by tranquil endurance of discomfort.

The price is obviously aimed at the American pocket. Even before devaluation it would have been expensive; at the present rate of exchange, it is exorbitant.

"Tuberculosis in Obstetrics and Gynaecology." By GEORGE SCHAEFER, M.D., F.A.C.S., F.I.C.S. Pp. xvi+307, with 58 illustrations. J. & A. Churchill, Ltd., London, 1956. Price 63*s*.

APPARENTLY, it is now two decades since the publication in English of a book on tuberculosis as it relates to obstetrics and gynaecology. In the interim, astronomical advances in therapeutic methods have altered the whole prospect of treatment. Dr. Schaefer is exceptionally well qualified to assess progress at this time because of his well-known work in this field, and his carefully selective abstraction of the literature. Until recently, this problem was still a controversial one. It is already obvious, however, that a remarkable measure of unanimity exists, even among experts, on treatment methods, although some aspects remain unsettled and require further study. It is difficult to take up the cudgels with the author on any major issue for his observations are well supported by substantial evidence from personal experience, or culled from the literature. The only exception perhaps is the chapter dealing with the choice of procedure for therapeutic abortion. Here, observations are made which are unwarranted by the statistical evidence presented. This, however, may be the result of circumstances, for, as a consequence of progress made, termination of pregnancy is now rarely, if ever, necessary. It is a little surprising also to find no mention of the controversial pathological entity which does rarely affect the genital tract and might easily be confused with tuberculosis, namely, sarcoidosis. Otherwise this excellent chapter on the pathology of the disease as it affects the genital tract is exhaustive. Other chapters worthy of special mention are those dealing with laboratory aids in diagnosis and the use of antibiotics in treatment.

Throughout, the text is concise, yet all major recent contributions are included without recourse to long historical surveys of outdated facts and figures. Generously illustrated and obviously very carefully planned, this book will remain an authoritative text on the subject for at least two decades to come; unless further progress demands another edition sooner. It is highly and confidently recommended to all who are interested in the management of tuberculosis in women. It is indeed worthy of a prominent place on the library shelf of every practising obstetrician and gynaecologist and should prove an invaluable aid to all who are preparing themselves for higher examinations in these subjects.

"Integrated Gynecology." By I. C. RUBIN, M.D., formerly Clinical Professor of Obstetrics and Gynecology, New York University, and JOSEF NOVAK, M.D., Professor of Obstetrics and Gynecology, University of Vienna, and formerly Clinical Professor of Gynecology, College of Physicians and Surgeons, Columbia University. Vol. 1, pp. 589; Vol. 2, pp. 496; Vol. 3, pp. 682. 218 figures. McGraw Hill, London, 1956. Price £22 10*s*.

THIS three-volume treatise is a new and major contribution to gynaecological literature. As the title suggests, the subject matter extends beyond pure gynaecology to embrace related subjects: thus, urology, endocrinology, reproductive abnormalities such as "intersex" and related problems, are some of the subjects dealt with in detail. Each chapter is followed by a massive list of references; for the chapter on physiology, for example, this amounts to no less than 31 pages of closely listed titles.

At first sight this publication might seem almost too formidable for any busy gynaecologist to handle—far less to read comfortably. But on further acquaintance this impression is quickly dispelled. The printing is large, and the page size relatively small; the illustrations are lavish and clear, and—above all—the text is simple and straightforward in style, making the reader's task not only easy but pleasant.

In a book so comprehensive it is difficult to single out any individual portion for special comment. The scope of the subject matter may be judged from the following titles and sub-titles (abbreviated) which show how only one subject is dealt with—namely, Vaginal and Vulval Inflammation: *Schizomycetes; Tuberculosis; Gonorrhoea; Syphilis; Ulcus molle; Granuloma Inguinale; Ulcus Vulvae Acutum* (*Lipschütz*); *Diphtheria; Fusospirochetal Infection; Colpohyperplasia Cystica* (*Colpitis Emphysematosa*); *Exfoliative Vaginitis; Herpes Genitalis; Molluscum Contagiosum; Verruca Vulgaris and Condylomata Acuminata; Vulvitis Aphtosa* [sic]; *Lymphogranuloma Inguinale; Variola, Vaccinia, Varicella and Measles; Actinomycosis; Moniliasis; Dermatomycoses; Trichomonas Vaginitis; Helminthiasis; Bilharziasis; Nemathelminthes; Pediculosis Pubis; Scabies*. All this occupies 62 pages of text followed by 17 pages of bibliography. Like all other sections this one is profusely and very clearly illustrated; there can be few gynaecologists who could browse over the pages without finding something new and something of interest.

The operative section is thorough but tends to be encyclopaedic, and operations are described that some workers might well regard as being of historical interest only. Here and there the authors' preference is noted, but not, perhaps, with sufficient emphasis to guide the inexperienced worker, or to dissuade an ambitious operator from embarking on a possibly unsatisfactory or difficult type of operation. Many of the very numerous and excellent illustrations in this section are from the standard German books on operative surgery.

This 3-volume book is undoubtedly a most valuable production, and one which reflects a vast amount of clinical experience and life-long study on the part of the authors. It is, and will long remain, a fruitful reference for

the gynaecologist who wishes to make a detailed study of some particular aspect of his specialty.

And here I make my one serious criticism. Are the authors in earnest, or do they "have the tongue in the cheek" when they state "The book was primarily designed for use by medical students and general practitioners"? If this statement is intended to be taken seriously, what would the authors consider to be a book suitable for the specialist?

J. Chassar Moir

REVIEW OF CURRENT LITERATURE

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PREGNANCY

1. Notes from the Diary of a Field and Hospital Surgeon, C.S.A.

By L. G. Capers. *West. J. Surg. Obstet. Gynec.*, **64**, 579–580. Oct. 1956.

This is a reprint of a short paper that appeared in 1874 concerning an incident in the American Civil War. A bullet passed through the testis of a soldier and then penetrated the abdomen of a female spectator who was nearby. Both of the wounded persons survived and 280 days after being wounded the girl delivered a full-term infant. About 3 weeks later the child was noticed to have a hard swelling in its scrotum and operation revealed the bullet which had pierced its mother's abdomen. To complete the story the two principals were introduced to each other, married and lived happily ever after.

[The editorial commenting on this reprint cites a similar case recounted but not published by Harvey Cushing.] *D. C. A. Bevis*

2. An X-ray Pelvimetric Study of Relaxin Extract in Pelvic Expansion.

By A. Weinberg. *Surg. Gynec. Obstet.*, **103**, 303–306. Sept. 1956. 2 figs. 5 refs.

This is the report from New York of an investigation of the role of the third ovarian hormone of pregnancy, relaxin, in producing pelvic expansion.

Four non-pregnant women of child-bearing age and 11 pregnant women in the middle trimester were given relaxin (releasin) intramuscularly over a period of 1 to 5 days, for a total dosage equivalent to 100 mg. of a relaxin standard. In the case of the non-pregnant, oestrogen in the form of premarin (2·5 mg. twice daily) was given for 2 weeks prior to the administration of relaxin.

X-ray pelvimetry was performed before the series of injections and 12 hours after the last injection. In no case was there evidence of increased separation of the symphysis pubis or increase in the transverse diameter of pelvic inlet, mid-pelvis or outlet.

The author concludes that relaxin extract, active for a relatively short period of time, is not a significant factor in causing separation of the symphysis or pelvic expansion. *John P. Erskine*

3. Simple Clinical Test for the Diagnosis of Early Pregnancy.

By G. D. Matthew. *Brit. med. J.*, **2**, 979. Oct. 27, 1956. 1 ref.

In a previous investigation the occurrence or not of withdrawal bleeding following the administration of parenteral oestrogen and progesterone was found to be an accurate test of pregnancy in a group of women of child-bearing age complaining of short-term amenorrhoea.

A further investigation has been carried out in similar circumstances but using oral oestrogen and progesterone. One tablet of "orasecron" (0·05 mg. Ethinyloestradiol with 10 mg. Ethisterone) was given three-hourly over two consecutive days so that a total dose of 0·5 mg. Ethinyloestradiol and 100 mg. Ethisterone was administered. A few patients complained of mild nausea.

A total of 94 patients were tested—about 64 per cent of them within 14 days of having missed a period. In no case was the period of amenorrhoea over 16 weeks. There was no withdrawal bleeding in 62 cases and all these women were later proved to be pregnant. In the remaining 32 cases uterine bleeding occurred within 14 days—within 7 days in 78 per cent of cases. Follow-up examination excluded pregnancy in each of these patients.

The author concludes that the oral administration of combined oestrogen and progesterone in the dosage prescribed would appear to constitute a reliable clinical method of diagnosing early pregnancy.

R. W. Grayburn

4. **Biologically Prolonged Pregnancy. Unexplained Foetal Deaths in the Neighbourhood of Theoretical Full Term and True Post Mature Cases of Pathological Type.** (Les grossesses biologiquement prolongées. Morts inexpliquées du foetus au voisinage du terme théorique et grossesses prolongées vraies de type pathologique.)

By H. PIGEAUD and R. CATTIN. *Gynéc. Obstét.*, **55**, 113–126. 1956. 6 figs.

The writers (from Lyons) refer to the work of Ezes in 1952 and that of Levy-Solal, Ninkowski and Morin, who followed up in the same year the work of Walker in Great Britain and considered the matter of postmaturity at the Congress in Algiers. Up to 1956 in Professor Pigeaud's service at Lyons each year about 15 babies died *in utero* at about full time for no evident cause.

The writers consider that in these cases the placentae show signs of senility. The recent work of Walker and others suggests that progressive anoxia of the foetus is the cause of death.

The authors report four histological findings which might account for this:

(*a*) Obliteration of the vessels in the villi, due to a parietal vascular lesion or to thrombosis. This may result in internal changes in the form of sclerosis of the stroma within villi or external changes outside the villi.

(*b*) Deposits of fibrin-like substance in the periphery of the villi (Langhans and syncytial layers).

(*c*) Alterations in the stroma of the villi—collagen formation preceding sclerosis.

(*d*) Alterations in the maternal aspect of the placental site which include vascular degeneration, minute infarcts, and evidence of inflammatory lesions.

The writers form the hypothesis that many of the unexplained foetal deaths in these cases are due to either abnormal speed of or degree of placental senility or failure of onset of labour when the patient is "ripe", or to a combination of these two.

The therapeutic success that has followed induction of labour 15–25 days before term in cases with a history of unexplained death *in utero* at about full time in preceding pregnancies, seems to support this hypothesis.

D. Maxwell

5. **Postmature Pregnancy: A Clinical and Pathologic Appraisal.**

By R. E. L. NESBITT. *Obstet. Gynec.*, **8**, 157–166. Aug. 1956. 8 tables. 22 refs.

Gestation was prolonged to 294 or more days (postmature) in 11 per cent of 7,415 term pregnancies at Johns Hopkins Hospital (1950–1954). Two groups, designated as "mature" (6,603 cases) and postmature (812 cases) were compared. In all cases the onset of labour was spontaneous. Postmaturity was more frequently seen in non-white patients, in primigravidae, and in the older age groups, the relationship being very marked over age 40.

Contracted pelvis, foetal distress, uterine inertia, prolonged labour, breech presentation and post-partum haemorrhage are significantly more frequent in postmature cases, and probably also prolonged second stage of labour and foetal anomalies. The foetuses were classifiable as "no heart beat, no respiration" and "poor condition" in a much higher percentage of postmature than mature cases. Postmature foetuses were slightly larger than mature ones, but the weight differential was not sufficient to account for the increased mortality among postmature cases.

There is a threefold increase in the postmature perinatal mortality rate over the control group, the most marked feature being foetal death occurring in labour. In this group the mortality was particularly high among non-white primigravidae over age 25.

The answer to the problem is not in the routine indiscriminate induction of labour but in the anticipation and prompt management of complications in labour.

[In 1955 (*Obstet. Gynec. Surv.*, **10**, 311) the author wrote a masterly review of prolongation of pregnancy. He showed that whilst numerous authors believed that the foetal death rate was increased in postmaturity, there were many authors who believed that the findings were inconclusive or contradictory. It is, therefore, very significant that in this reappraisal of the subject, Nesbitt plumps down firmly on the side of the former group.]

J. G. Dumoulin

6. **Ante-Natal Care and the Prevention of Eclampsia and Severe Toxaemia.**

By T. DIXON HUGHES. *Med. J. Aust.*, **2**, 48–50. July 14, 1956. 2 tables. 9 refs.

The incidence of eclampsia among "booked" patients at The Women's Hospital (Crown Street) since June, 1948 is 1 in 3,927. For this to be achieved, it is necessary for the whole staff, medical and nursing, to exercise eternal vigilance for the early warning signs of toxaemia throughout the antenatal period. It is necessary that the

population be educated, so that they appreciate the need for adequate antenatal care. Medical attendants must properly evaluate the blood pressure readings in particular as to their individuality and relativity. Most figures reveal that at least 75 per cent of patients who develop severe toxaemia show excess gain of weight. A weight increase of over one pound per week must be checked within 7 days, and if the weight increase is associated with a relative rise in blood pressure, irrespective of successful weight control, the patient must be examined weekly. The diet given is of 2,200 calories with approximately 85 grammes of protein. Advice is given not to ingest an excess of fat and carbohydrate, and after the fifth month salt is restricted. If albumin is found in a catheter specimen of urine, the patient is admitted to hospital for the determination of its cause. The average number of antenatal visits per patient is 15. A check is made of the antenatal record card after each visit, and if anything has been overlooked, contact is made with the patient.

During the period 1947–1948, 50 per cent of the toxaemias were severe, whereas in the period 1953–54 with improved antenatal care, it was 21 per cent. In 1947 the incidence of eclampsia was 1 in 400 and the premature neonatal death rate from all causes was 15·6 per cent, while over the last five years the incidence of eclampsia has been 1 in 5,000 and the average premature neonatal death rate has been 10·3 per cent.

S. Devenish Meares

7. Influence of Vitamin B_6 on the Incidence of Eclampsia.

By M. WACHSTEIN and L. W. GRAFFEO. *Obstet. Gynec.*, **8**, 177–180. Aug. 1956. 1 table. 23 refs.

Four hundred and ten women received 10 mg. of pyridoxine hydrochloride daily during pregnancy. This group was compared with a similar control group. The authors believe that there is a disturbance of vitamin B_6 metabolism in women with normal pregnancy which is even more marked with toxaemia.

There was a statistically significant reduction of pre-eclampsia in the treated group. The incidence of pre-eclampsia was 4·4 per cent in the control and 1·7 per cent in the treated group. *J. G. Dumoulin*

8. Rôle of Adrenal Cortex in the Causation of Toxaemia of Pregnancy.

By R. K. K. TAMPAN, K. SUNDARAM, and C. P. CHAMUKUTTAN. *J. Obstet. Gynaec. India*, **7**, 1–14. Sept. 1956. 21 refs. 2 figs.

In this article, sponsored by the Madras State Research Committee, an attempt is made to study the role of the adrenal cortex in the causation of toxaemia of pregnancy. Seven small groups of women were studied, comprising non-pregnant women, normal cases before the thirty-fifth week of pregnancy and after, normal and toxaemic post-partum cases, and women with mild and severe toxaemia. Each group was subjected to a series of 10 biochemical tests, and an eosinophil count. The following conclusions were drawn.

In toxaemic women the sodium-ion is retained in the blood to a greater extent than is the case in non-toxaemic women, and the more severe the toxaemia, the less sodium is excreted in the urine. There is a retention also of blood potassium in toxaemia. Post-partum the excessive amounts retained of both sodium and potassium are excreted in the urine.

The level of blood chlorides was shown to be higher in toxaemic than in non-toxaemic cases, and post-partum the chloride excretion was shown to be greater in the former cases.

Studies of the excretion value of total corticosteroids in the urine showed higher levels to be present in toxaemic women than in non-toxaemic women. Eosinopenia varied according to the level of corticoids excreted in the urine.

The Vanderbilt co-operative study on nutrition is quoted as suggesting that there is a dietetic deficiency among pre-eclamptic women, and it is suggested that this deficiency (especially of the vitamin B complex) may lead to hypertrophy of the adrenal cortex. This would lead to an excessive liberation of corticosteroids. This excess in turn leads to degenerative placental changes, with the resultant liberation of an enzyme which, together with the excessive corticosteroids, causes vasospasm and oedema.

It is concluded that adequate amounts of Vitamin B complex should be given to pregnant women before the placenta is formed, in order to avoid pre-eclampsia and eclampsia. Once established, it is conceded that the disease can only be treated symptomatically.

John McKiddie

9. Adrenal Function in Pregnancy.

By N. S. ASSALI. *West. J. Surg. Obstet. Gynec.*, **64**, 567–569. Oct. 1956. No refs.

The author gives a brief review of current concepts in this subject. Many different hormones are secreted by the suprarenal cortex and may be grouped into the categories: glucocorticoids, androgenic steroids, mineralocorticoids, oestrogenic·steroids and progestational steroids. Very little is known of the last two groups and they are not discussed further. Adrenocortical function in the human is complicated by the presence of the placenta, producing an abundant supply of steroid hormones and modern methods are inadequate for the detection of increased secretion by either the anterior pituitary or the adrenal cortex. Evidence recently gathered seems to indicate that the placenta can produce ACTH-like substances and also several adrenocortical-like hormones; this may explain the improvement in certain collagen diseases during pregnancy. Study of the plasma level of certain of the adrenal hormones seems to show that activity of the adrenal rises during pregnancy reaching a peak at the end of gestation, following delivery there is a fall to the non-pregnant level. There is only meagre evidence that the toxaemias of pregnancy may be due to increased adrenocortical activity. *D. C. A. Bevis*

10. Investigation into the Problem of Late Abortions from 4 to 7 Months of Pregnancy.

By H. V. TILAK. *J. Obstet. Gynaec. India.* **7**, 15–30. Sept. 1956. 10 refs.

An enquiry sanctioned by the Indian Council of Medical Research showed that approximately 45 per cent of abortions admitted to hospitals in Bombay occurred between the fourth and seventh months of pregnancy. The incidence is three times as high as that found in Western countries. It is claimed by the author that, by systematic enquiry, the cause of the abortion could be ascertained in 25 per cent of cases, and that by more detailed investigation the cause could be found in 52 per cent of cases. In the remaining 48 per cent, "devitalizing factors" are enumerated as being contributory causes to the miscarriage.

The abortion rate is said to be 7 times higher in cases where the husband has defective spermatogenesis. Physical trauma to the mother was blamed in many cases, and in others there was a congenital defect in the foetus. Twins were 6 times more common in late abortions than in full-time deliveries. Defects of the cord were alleged to be responsible for 16 per cent of foetal deaths, while pathological placentae were found 12 times more often in cases of late abortion than in full term deliveries. The Rhesus factor played no part in late miscarriages.

In cases in which the abortion was not attributed to any definite cause, diseases in the mother such as anaemia and hyperemesis, are quoted as being devitalizing factors which predispose to late abortions.

[In all, 707 consecutive cases were examined, but the same investigations were not carried out in every case.]

John McKiddie

11. **Epigastric Pain in Pregnancy Toxemias. A Report of Fatal Peptic Ulcers in Toxemias.**

By C. F. LANDMADE. *West. J. Surg. Obstet. Gynec.*, **64**, 540–544. Oct. 1956. 11 refs.

Acute epigastric pain is an early and reliable symptom of pregnancy toxaemia but little reference has been made to its basic pathology in the literature. The author studied autopsied cases of peptic ulcers in pregnancy and reports 2 cases of his own. One patient had eclampsia at the 37th week of her 2nd pregnancy and died on the 11th day of the puerperium after haematemeses and bleeding per rectum. Autopsy revealed a perforated acute ulcer in the first part of the duodenum, the liver being fairly normal. The second case also had eclampsia and died on the day following Caesarean section; autopsy showed a fairly normal liver and a large perforation in the cardiac portion of the stomach. The records are reviewed of 31 patients who died in the Los Angeles County General Hospital; these patients all had severe pre-eclampsia or eclampsia and all had some degree of ulceration of the upper gastro-intestinal tract. The lesions are not thought to be due to uraemia or post-mortem change and the author considers that they cause the epigastric pain in many instances.

D. C. A. Bevis

12. **Successful Pregnancies after Spontaneous and Induced Abortions. Clinical, Statistical and Social Study of Pregnancy Wastage in Five Hundred and Five Private Patients.**

By M. P. WARNER. *West. J. Surg. Obstet. Gynec.*, **64**, 504–514. Sept. 1956.

The author presents her results over 25 years in New York; 413 of the patients had 1 abortion and 44 had 3 or more; 241 of the women had induced abortions and a further 32 had therapeutic terminations. No further live pregnancies were obtained in 58 per cent of the spontaneous group and in 70 per cent of those who had illegally induced abortions. Medical treatment was undertaken for secondary sterility in 92 per cent of the patients, only 3·3 per cent had had primary sterility before the abortion (only 27 patients were treated for more than 2 years). The author gives an exhaustive review of her methods of treatment which resulted in 126 live pregnancies after the abortions; tubal insufflation and semen analysis are always carried out and pelvic pathology of all degrees energetically treated, retroversion and the Rhesus factor are not considered important factors in either the abortions or in the subsequent sterility.

[This is a long and involved paper and the author's conclusions are not always clear; in some instances the timing of her procedures and the results obtained leave something to be desired.]

D. C. A. Bevis

13. **Research into the Foetal Electrocardiograph in the Course of Pregnancy and Labour.** (Recherches d'électrocardiographie foetale au cours de la gestation et du travail.)

By C. SUREAU. *Gynéc. Obstét.*, **55**, 21–33. 1956. 11 figs. 21 refs.

Following studies of the electro-uterogram in the Port Royal Maternity Hospital, Paris, the writers have attempted to work out a similar technique for the electrocardiograph in the foetus.

A portable electro-encephalograph machine was used with 4 pens registering directly. Two types of electrodes were used—cutaneous monopolar or tripolar and endo-uterine. The latter were introduced through the cervical canal into the uterine cavity, outside the membranes if they were intact. No untoward incident such as infection, perforation of the uterus or damage to the foetus occurred in any of the 34 cases, nor were the membranes ruptured accidentally in any case. There was nothing to show that the intra- or extra-amniotic position of the electrodes had any bearing on the tracings.

During pregnancy the vitality of a doubtful foetus can be verified without doubt. The writers do not feel that electrocardiography should be used for diagnosis of presentation although they could demonstrate differences between breech and vertex cases. Their series included two cases of twins confirmed by two different electrocardiographic rhythms.

The writers consider foetal electrocardiography is useful for the diagnosis of foetal distress. They showed that cardiac activity continued during contractions, only in one case out of 45 did they note slowing during contractions. The average foetal heart rate was in the region of 140 per minute. They also studied the cardiac rhythm during the intravenous instillation of pitocin. In a series of 17 observations no change in the rhythm was noted.

D. Maxwell

14. **Defective Blood Coagulation Associated with Intrauterine Foetal Death.**

By J. M. FARRAR. *Med. J. Aust.*, **2**, 65–68, July 14, 1956. 2 figs. 11 refs.

This is a report from King George V Hospital, Sydney, of a case of fibrinolysis probably associated with hypofibrinogenaemia occurring in an Rh-negative multipara with anti-Rh agglutinins, whose foetus had been dead for 11 weeks. Labour was induced by pitocin drip administration, and haemorrhage commenced 3 hours after the onset of labour, the blood failing to clot. A modification of Scott's test was used to confirm this, an unstable clot was formed which re-dissolved in fifteen minutes. Three grammes of fibrinogen were given intravenously and the foetus, intact sac, and placenta were expelled one and a half hours after the initial haemorrhage. A further gramme was given one hour after delivery.

Farrar discusses the aetiology, clinical features, diagnosis and management of hypofibrinogenaemia and fibrinolysis in obstetrics. He believes that in the presence of a dead foetus, which is not expelled, labour should be induced by pitocin within four weeks of its death, so as to avoid the potential dangers of fibrinolysis and hypofibrinogenaemia. These conditions result from uterine contractions forcing the substances initiating the disordered coagulation mechanism into the circulation from the autolysed placenta.

S. Devenish Meares

15. **Treatment of Megaloblastic Anaemia of Pregnancy and the Puerperium with Vitamin B_{12}.**

By E. B. ADAMS. *Brit. med. J.*, **2**, 398–400. Aug. 18, 1956. 24 refs.

It seems likely that there are several varieties of megaloblastic anaemia associated with pregnancy and the puerperium. This paper records the results of a clinical trial using large doses of vitamin B_{12} in 10 cases of the type of this condition seen in Durban. Seven of the cases concerned post-partum patients. Three were treated before delivery. The clinical features and bone marrow appearances are briefly described.

All cases were observed for a control period before treatment was started. Vitamin B_{12} was administered by the intramuscular route in doses varying from 100 μg. given in one injection to 1,400 μg. in daily injections of 100 μg. Progress was determined by daily reticulocyte counts and by estimations every five days of haemoglobin and packed cell volume.

Response was satisfactory in all seven cases treated after delivery and was as good with doses of 100 μg. as it was when 1,000 μg. or more was given, the average daily haemoglobin rise being 0·16 g. per 100 ml. The three antenatal cases responded poorly. In another series, better results were obtained by using folic acid.

Although several varieties of megaloblastic anaemia of pregnancy and the puerperium occur, they all have much in common. They tend to occur during the last three months of pregnancy and in the puerperium; the peripheral blood picture is inconsistent; spontaneous remission may occur after delivery; dietetic deficiencies do not appear to be the only cause. It has been suggested that during pregnancy, a resistance to the action of haemopoietic substances develops.

R. W. Grayburn

16. **Hiatus Hernia in Pregnancy.**

By W. T. MIXSON and H. J. WOLOSHIN. *Obstet. Gynec.*, **8**, 249–260. Sept. 1956. 4 figs. 2 tables. 34 refs.

Oesophageal Hiatus Hernia in Pregnancy.

By C. G SUTHERLAND, J. C. ATKINSON, B. G. BROGDON, N. E. CROW and W. E. BROWN. *Obstet. Gynec.*, **8**, 261–264. Sept. 1956. 1 fig. 3 tables. 7 refs.

Although the symptom complex of hiatus hernia in pregnancy may vary, a pattern can be recognized. The patient is usually a multipara somewhat older than most women bearing children. Heartburn is usually present, beginning between the sixteenth and twenty-second week of gestation: the episodes become progressively more severe and frequent as pregnancy progresses. It is made worse by lying down and may interfere with sleep. Sitting up, standing, or sleeping with head and shoulders elevated usually give relief. It may become worse after meals. The heartburn may be relieved by belching or vomiting, by the use of antacids or diet. Nausea and vomiting are less characteristic. The patient is free of symptoms between pregnancies. These are the opinions of Mixson and Woloshin. The second paper by Sutherland and his colleagues states that vomiting is the most common symptom: epigastric pain and haematemesis may also be found.

The first contribution is a study of 360 pregnant women in whom 31 oesophageal hiatus herniae were found. The second report concerns 92 patients taken at random, 20 of whom were found to have herniae.

The progressive enlargement of the uterus as gestation advances is significant in the aetiology of hiatus hernia, and the hernia usually disappears after delivery. Sutherland *et al.* consider that whilst symptoms disappear post-partum the herniae persist in 36 per cent of cases.

Conservative medical measures are usually sufficient to improve symptoms until delivery takes place. Surgical repair and other drastic procedures are rarely necessary.

J. G. Dumoulin

17. **Thyroid Disease in Pregnancy: Its Detection and Management.**

By K. P. RUSSELL. *Obstet. Gynec.*, **8**, 207–212. Aug. 1956. 3 figs. 13 refs.

Measurement of thyroid function by the determination of the basal metabolic rate shows that in pregnancy in the normal patient the BMR shows a gradually increasing rate up to +20 at the ninth month. This represents the augmented basal metabolism associated with increasing foetal and maternal tissue masses as pregnancy advances. Estimation of the protein-bound iodine of the serum or plasma in pregnancy shows a similar elevation but with a wider fluctuation and occasional very high readings. Determination of the behaviour of radio-active iodine (I^{131}) in the body after ingestion is not at present a satisfactory test in pregnancy since the foetal thyroid tissue

has a great avidity for the isotope. Cholesterol determinations are not applicable as thyroid-function tests during pregnancy.

Hypofunction of the thyroid is either masked or temporarily corrected during pregnancy by increased thyroid activity. In the study of infertility and habitual abortion, however, the above tests may be helpful, as also may be the "thyroid-stimulating-hormone test".

The diagnosis of hyperthyroidism in pregnancy must remain a clinical one, for the above tests are not helpful. Of the 3 methods of treatment—antithyroid drugs, radio-active iodine, and surgery—the latter is usually the method of choice.

Many pregnant women show diffuse thyroid enlargement during pregnancy. A hitherto unsuspected nodule may become detectable. The incidence of cancer in such nodules is 10–20 per cent so that they should be removed. Simple non-toxic colloid goitre has no influence on pregnancy and usually responds to small doses of thyroid extract.

J. G. Dumoulin

18. **Pheochromocytoma in Pregnancy.**

By W. C. Brann, W. G. Puryear and R. L. Landes. *J. Urol.*, **76**, 323–329. Oct. 1956. 2 figs. 6 refs.

A Negress, aged 30, 8½ months pregnant, was admitted to hospital on account of severe headache. Five previous pregnancies were uneventful. The blood pressure on admission was 140/80, but during a severe bout of headache it rose to 300/170. The headaches were accompanied by sweating. Phaeochromocytoma was suspected, and a Caesarean section performed under spinal anaesthesia. The blood pressure did not fall during the operation below 120/80.

Exploration of the right kidney area revealed a lump about the size of an orange. Massage of the lump caused the blood pressure to mount to 180/130, massage of the left suprarenal area produced a blood pressure of 260/160. The reason for this was not understood, and it was suggested that a double phaeochromocytoma might be present, but soon after the operation an intravenous pyelogram was performed, and apart from a displacement outwards of the first two inches of the right ureter, no abnormality was seen.

The tumour was removed through a loin incision, and was found to be medial to the lower pole of the kidney with the ureter passing over it. The blood pressure, which was stable during the operation, fell to 70/50 when the tumour was removed, and soon was unobtainable. Although blood was given under pressure, and levophed, 4 mg. per litre intravenously, 20 minutes elapsed before the pressure reached 60/40. Post-operatively there was oliguria, wound sepsis, and thrombophlebitis at the injection sites. Levophed was maintained for four days.

Forty cases have been collected from the literature, in nine symptoms became fulminant between onset of labour and 24 hours post-partum. Eight of the patients died. The common symptoms are headache, vomiting, nausea, sweating, palpitation and blanching.

[The dangers of confusing this type of case with essential hypertension in kidney disease and with toxaemia in pregnancy are obvious. In this connexion it is important to remember that in 37 out of 51 cases collected by Green (*J. Amer. med. Ass.*, 1946, **131**, 1260) the hypertension was persistent and not paroxysmal.

The tumour in the case described was not in the suprarenal area and probably arose in a retro-peritoneal ganglion. The pyelogram revealed no downward displacement of the kidney, and the pelvis and calyces had the same appearance that one would find at that stage of pregnancy. The only deformity was the outward displacement of the upper two inches of the ureter. It was, therefore, satisfactory that the tumour had been located at the time of Caesarean section.

The methods of investigation are described, but no mention is made of the value of a raised metabolic rate. These cases are not very common, and close study of the paper is advocated.]

J. H. Carver

19. **Malignant Diseases Associated With Pregnancy.**

By H. C. Hesseltine and M. F. Loth. *West. J. Surg. Obstet. Gynec.*, **64**, 529–535. Oct. 1956. 9 refs.

The authors review 33 cases of malignancy in pregnancy occurring at the Chicago Lying-In Hospital. There were 25 carcinomas, 12 being in cervix, 6 in breast and 4 in the rectum or colon. Eight sarcomas included 4 cases of Hodgkin's disease. Ages varied from 14 to 46, the Hodgkin's disease accounting for the youngest patients. Seventeen of the 33 patients survived 5 years, results being best with cervical carcinoma (50 per cent) and the rectum-colon cases; only 1 patient with carcinoma of the breast survived 5 years. Treatment is briefly reviewed and the authors conclude that whenever the malignancy is discovered during pregnancy the appropriate treatment should be promptly instituted. Treatment of cervical carcinoma in early pregnancy may destroy the foetus but it may escape major harm; in late pregnancy proper irradiation is less likely to injure the foetus. Therapy for malignancy of the breast, colon, etc., should be started at once in accordance with the usual methods and although risk to the foetus does occur, care for the mother requires vigorous steps. Radio-iodine should not be used for carcinoma of the thyroid as it can cross the placental barrier and destroy the foetal thyroid, other methods of treatment should be used until the child is viable when pregnancy should be terminated and isotope therapy instituted.

D. C. A. Bevis

20. **Cancer of the Cervix and Pregnancy.**

By H. C. McDuff, W. I. Carney and G. W. Waterman. *Obstet. Gynec.*, **8**, 196–202. Aug. 1956. 2 figs. 8 tables. 14 refs.

In the past 25 years 16 cases of cancer of the cervix have been treated during pregnancy at Rhode Island Hospital, Providence. The condition occurs about once in 2,000 obstetric cases, usually in a multipara. In 62·5 per cent abnormal bleeding occurred, and 25 per cent had no symptoms at all.

The authors suggest the following schedule of treatment: (*a*) First trimester—X-ray, spontaneous abortion,

radium; second trimester—abdominal hysterotomy, X-ray, radium; third trimester—classical Caesarean section, X-ray, radium; fourth trimester—radium followed by X-ray. (*b*) Radical hysterectomy combined with pelvic node dissection can replace treatment in any trimester, providing the case is favourable. (*c*) Consideration should be given to the transperitoneal node dissection following emptying of the uterus in the second and third trimesters.

The authors report a survival rate of 56 per cent. Pregnancy does not seem to hasten or worsen the clinical course of the disease.

J. G. Dumoulin

21. **A Case of Tubal Pregnancy Due to Endometriosis.** (Ein Fall von Tubenschwangerschaft, verursacht durch Endometriose.)

By A. Wist. *Gynaecologia, Basel*, **141**, 298–304. May 1956. 4 figs. 4 refs.

Up to 1954 only 39 cases of tubal pregnancy with tubal endometriosis have been described, and of these 5 were by this author. In two-thirds of the cases the pregnancy was interstitial, in only 3 ampullary, and the rest at the junction of the isthmus and interstitial portion of the tube.

In this paper the author describes another case. The patient aged 32 years, after 6 years sterility had a laparotomy because of a ruptured tubal pregnancy. About five pints of blood were removed from the peritoneal cavity. The left tube was adherent to surrounding tissue but the fimbria was free and the abdominal ostium open. Between the isthmus and interstitial portion of the tube there was a thumb sized swelling with a small opening at the upper pole through which blood oozed. The right tube was adherent with a deformed ampulla and closed abdominal ostium.

The left tube was removed and examined histologically. This showed a normal ampulla with healthy mucosa but there was some round cell infiltration and excessive connective tissue in the tubal wall, obviously the result of old mild inflammation. This was less marked at the isthmus but there decidual cells were found. At the proximal part of the isthmus the wall showed typical endometriosis and there was an endometrial polyp practically filling the tubal lumen. From here there was no communicating channel to the uterus, the tube being destroyed and filled with chorionic tissue and blood. However, at the uterine cornu the lumen was open.

The author considers that this is a case of tubal pregnancy due to tubal endometriosis and claims that endometriosis is a common cause when the pregnancy is interstitial or near the junction of the isthmus and interstitial parts of the tube. It is not a common cause when the pregnancy is ampullary, a much commoner site.

Jean L. Hallum

LABOUR

22. **A Study of the Electrical Activity of the Uterus in the Course of Labour.** (Etude de l'activité électrique de l'utérus au cours de travail.)

By C. Sureau. *Gynéc. Obstét.*, **55**, 153–175. 1956. 21 figs. 1 ref.

In the Port Royal Hospital, Paris, the author carried out continuous electrical hysterography on 51 women throughout their first stages of labour. Controls were obtained by similar examination of 24 women who were not in labour. The apparatus used was a modified electro-encephalography instrument using 4 pens registering directly. Three types of electrodes were used: monopolar cutaneous, tripolar cutaneous and endo-uterine. These last were introduced into 34 labouring women by the cervical canal. In 16 cases they were placed in the amniotic cavity after the membranes had ruptured, and in 13 cases between the intact membranes and the uterine muscle. On 5 occasions the electrodes were placed outside the membranes after rupturing them. The depth of insertion of the electrodes varied and 87 tracings were studied. There were no ill effects from the passage of the instruments. The paper classifies the tracings, and many of them are reproduced with detailed annotations.

The writer draws attention to the difference in electrical activity at various points in the anterior wall of the uterus when various pairs of electrodes are used. There are considerable differences in electrical activity of the anterior and posterior walls of the uterus; these have been made evident by simultaneous electromyographic methods using cutaneous and endo-uterine electrodes. The report gives an account of certain paradoxical observations with one pair of cutaneous electrodes which had the characteristics of what the author calls "electrical inertia".

The author hopes that he has shed some light on the relationship between uterine electrical activity and clinical phenomena in labour, but he states that owing to the small number of cases, the varying nature of them and the uncertainty of the technique, it would be unwise to draw many firm conclusions.

[The field of research in electrohysterography is vast: The first promising results of this technique in investigating the use of endo-uterine electrodes seem still to be increasing. These results should not allow readers to forget that the problem of dynamic dystocia is the problem of cervical physiology and that so far these electrical investigations have not solved it.]

D. Maxwell

23. **Induction of Labour.**

By L. G. H. van Dongen. *S. Afr. med. J.*, **40**, 959–964. Oct. 6, 1956. 5 tables. 10 refs.

The author discusses the history of surgical induction and the various methods of medical induction. The physiology of uterine action is still largely unknown. It is no longer believed that foetal activity plays any part in its onset, although Malpas points out that it is often delayed with an anencephalic foetus. The placenta wields considerable influence by production of hormones. Foetal bulk, as in multiple pregnancy, must play some part.

Labour is the culmination of the earlier Braxton Hicks contractions. Before the onset of labour pitocin will often produce strong regular contractions, which often ripen an uneffaced cervix. Towards term there is a gradual

reduction of progesterone-like substances. Oestrogens increase in concentration causing an increase in the glycogen, phosphocreatinine, actomysin, glutathione and calcium content of the uterus. The formation of the lower segment is discussed, and the author claims that rupture of the membranes enhances influences favourable to good uterine action.

The two main methods of induction in this series were the use of pitocin and rupture of the forewaters. Pitocin still has 4–7 per cent of the vasopressor factor, and this may cause occasional dangerous side-effects. A pure oxytocic factor, "Syntocinon", has been synthesized. This was used in 70 inductions and the effects and results were exactly similar to those of pitocin. At the Queen Victoria Hospital, Johannesburg, the oil, bath and enema routine is preceded by stilboestrol and is followed by pitocin either intermittently or by intravenous drip. The surgical method employed is rupture of the forewaters after the membranes have been stripped.

In 4 years there were 16,030 deliveries, and induction was performed in 850 cases (5·3 per cent). Toxaemia of pregnancy, postmaturity, premature rupture of the membranes, the presence of Rh antibodies, and intrauterine death were the indications in 95·5 per cent of the cases induced.

Pitocin has been found useful in preparing the cervix for surgical induction in cases of pre-eclampsia. Patients with eclampsia are induced 24 hours after the fits are controlled.

The author feels that if medical induction does not precipitate labour the patient is unlikely to be postmature. In such cases surgical induction is rarely performed. Of 301 patients induced for postmaturity 78 per cent were successful.

When Rh antibodies are present he believes that labour should be induced at 38 weeks gestation. Intrauterine death is treated by medical induction only and pitocin drip.

Of the patients induced 43 per cent were primiparae. The success rate was 87 per cent for primiparae and 88·5 per cent for multiparae. Fifteen patients (1·8 per cent) were induced before the 32nd week of pregnancy, and 778 (91·4 per cent) were beyond 36 weeks. The combination of pitocin drip and surgical induction was successful in 28 cases in which it was employed. Surgical induction alone was successful in 209 out of 232 cases (90 per cent). Pitocin drip was successful in 83 out of 136 cases (61 per cent), whereas ordinary medical induction was successful in 426 out of 898 cases (47 per cent).

Labour was prolonged beyond 24 hours in 31 cases (4·1 per cent). Post-partum haemorrhage occurred in 138 cases (18·5 per cent); the incidence was highest after pitocin drip (24 per cent) and lowest with the combined method of induction (7·2 per cent). Ergometrine was not given before the delivery of the placenta.

The one maternal death was in no way related to the induction. There were 47 stillbirths, 24 being macerated and 23 fresh. Not one of the stillbirths appears to have been caused by the induction. There were 22 neonatal deaths, 12 being due to prematurity and atelectasis.

L. J. Abramowitz

24. Natural Childbirth in the Treatment of Mothers with Pulmonary Tuberculosis. (L'accouchement psychophysique involuntaire des tuberculeuses pulmonaires en traitement.)

By A. NOTTER and G. EGRON. *Gynéc. Obstét.*, **55**, 87–99. 1956.

In this report from Lyons, the authors describe 253 cases, including 92 primigravidae and 161 multiparae. They conclude that as a general rule there is a marked reduction in the degree of pain, with a large number of completely painless first stages (23, including 4 primigravidae and 2 cases "B.B.A." among the multigravidae).

They also found that labour was shortened. The average duration of labour was 10 hours for primigravidae and 6 hours for multiparae. They noted that amongst the ill patients under sanatorium regime the average duration of labour was 9·25 hours for primigravidae and 5·10 hours for multiparae.

The writers attempt to explain these findings by the two factors classified by Grantley Dick Read and Nicolaiev, namely: (*a*) Physical action, which includes relaxation of the neuromuscular mechanism, the influence of perineal and cervical tone, and diaphragmatic blockage, and (*b*) Psychological action, which includes isolation from the family and home, an entirely optimistic outlook, and a new centre of interest created in the higher centres by a deviation of thought from that of labour towards that of tuberculosis.

D. Maxwell

25. Amiphenazole in Obstetric Analgesia.

By J. M. HOLMES. *Lancet*, **2**, 765. Oct. 13, 1956. 2 refs.

The author describes his experience in the use of morphine and amiphenazole during labour. He concludes that amiphenazole reduces the undesirable side-effects of nausea and vomiting due to morphine without significantly reducing its analgesic action. Neonatal apnoea was also reduced but not completely eliminated by the dosage of 30 mg. of amiphenazole given in combination with the morphine.

H. H. Fouracre Barns

26. Paracervical Block in Labor.

By D. W. FREEMAN, T. P. BELLVILLE and A. BARNO. *Obstet. Gynec.*, **8**, 270–277. Sept. 1956. 3 figs. 4 tables. 3 refs.

Paracervical block anaesthesia was used by the authors in 364 patients in labour. Six to 10 ml. of a local anaesthetic were injected into the lateral fornix of the vagina on each side at 3 and 9 o'clock positions. The needle used was encased in a guide so that its tip projected 1½ cm. beyond the guide. The blocks were performed at different times in the first stage, most of them when the cervix was 4–6 cm. dilated. Complete or nearly complete pain relief was obtained in 86 per cent of cases. A significantly higher percentage of effective blocks was obtained in the group in which the anaesthetic solution contained adrenalin. The longest duration of effect was obtained with xylocaine; the duration in the group ranged from 10 minutes to 3 hours with an average of 1 hour.

Paracervical blocks do not relieve the pain associated with distension of the lower vagina and vulva.

Depression of the foetal heart rate to 80–100 per minute was noted in 14 (3·7 per cent) cases. In all but 2 it returned to normal when oxygen was given to the mother.

The procedure is recommended as a simple, safe and effective method of relieving pain in the first stage of labour.

J. G. Dumoulin

LACTATION

27. **The Parenteral Use of Methallenestril for the Suppression of Lactation. A New Approach.**

By E. E. Napp, A. F. Goldfarb and G. Massell. *West. J. Surg. Obstet. Gynec.*, **64**, 492–496. Sept. 1956. 4 refs.

Relatively few women in the United States breast-feed their babies, and the authors, at the New York Medical College, have sought an effective method of suppressing lactation. Methallenestril, a synthetic oestrogen, 100 mg. intramuscularly given on the day of delivery, has proved most effective. Two hundred and seven patients were given the drug and 96 per cent had an adequate response. One hundred and ninety-three patients were treated without hormones as a control group, 39 per cent responding well; 213 patients treated with 45 mg. diethylstilboestrol after delivery, followed by 5 mg. three times a day for 3 days, gave a 90 per cent response. Withdrawal bleeding was minimal with methallenestril and there were no side effects. The authors are very impressed with the preparation.

D. C. A. Bevis

INFANT

28. **Newborn Non-European Infants: A Report.**

By R. McDonald. *S. Afr. med. J.*, **30**, 1035–1039. Oct. 27, 1956. 8 tables, 12 refs.

The author has made a study of 5,208 babies born in a 5-year period at St. Monica's Maternity Hospital, Cape Town. The average birth weight of Bantu babies was slightly more than that of Coloured babies. Weights in relation to parity and age were compared. The incidence of multiple pregnancy was 1 in 64 cases.

The prematurity rate in Bantu patients was 7·2 per cent, and in Coloured patients 13·3 per cent. The combined prematurity rate was 12·9 per cent. Survival rates in relation to weight are discussed, the total survival rate being 83 per cent. The causes of death are tabulated.

There were 208 stillbirths (39·9 per thousand). Of these 98 were emergency cases. There were 180 neonatal deaths (36 per thousand births).

The Wassermann test was positive in 36 cases. There has been a progressive reduction in the incidence of syphilis over the years.

There were 52 Rh-negative cases, and there were 4 cases of haemolytic disease.

J. Abramowitz

29. **Resuscitation of Newborn Infants. A Report by the Special Committee on Infant Mortality of the Medical Society of the County of New York.**

Obstet. Gynec **8**, 336–361. Sept. 1956. 104 refs.

This is a report by a committee of 24 members on the methods of preventing perinatal deaths from asphyxia, and ways by which its complicating effects could best be combated in those infants who survive.

Human foetal respiratory movements have been observed as early as the 12th week coincident with the interruption of the placental circulation. It is not known whether amniotic fluid is found in the lungs under physiological conditions or only in asphyxial states. It has been demonstrated that in the anoxic state the foetus can utilize glucose anaerobically. The neurochemical factors resulting from separation of the placenta and the existing level of excitability of the respiratory centres are largely responsible for the initiation of postnatal respiration. The inability of some premature babies to continue breathing after the prompt onset of respiratory movements is occasionally due to anoxia superimposed on immaturity of the pulmonary capillary bed.

Respiratory stimulants are adjuvants of limited value in the type of case where there is drug-induced depression of the respiratory centre. Alpha-lobeline is considered too dangerous and uncertain in action to warrant its use. Coramine is very weak and unreliable, and the toxic dose is too close to the therapeutic to make the drug safe to use. Picrotoxin, cardiazol and epinephrine are all dangerous and should not be used. N-allylnormorphine is still an experimental drug being tried out in depression due to morphia and pethidine: it is not a stimulant and in parturients given ether anaesthesia it appears to increase depression of the infant. The use of 50 per cent glucose intravenously in the anoxic infant deserves further study.

From the obstetric point of view the prevention of prematurity is important in lowering the incidence of foetal distress. In premature deliveries analgesics should be used sparingly and a wide episiotomy performed. In full-term infants difficult forceps deliveries should be avoided. The correct management of breech deliveries is most important. Babies delivered by Caesarean section should have gastric lavage.

The routine care of the neonate should include aspiration of the trachea with a rubber catheter with the infant in the head down position. Premature infants should not receive oxygen unless there is cyanosis or dyspnoea. Oxygen, if given, should not exceed a concentration of 40 per cent. The routine administration of vitamin K and antibiotics seems to be of value. The saturation of the environment with various amounts of water is widely used but has not been subjected to critical trial. Temperature should be maintained between 88° and 92° F.

The report emphasizes that the requirements laid down for mechanical resuscitators and inhalators used for initiation and maintenance of adequate pulmonary ventilation are confusing and emphasize the general lack of knowledge on the subject. Most of these requirements, on which comments are made, are more concerned with

the safety of the equipment than its effectiveness. The characteristics and applicability of the several mechanical aids used in resuscitation are listed, and principles for an ideal resuscitator are suggested although no machine at present fulfils all the conditions.

Further sections of the report are devoted to evaluation of pathological and statistical data, education and training of those responsible for resuscitation of newborn infants, and recommendations for research.

J. G. Dumoulin

30. **Neonatal Hepatitis.**

By C. ISAACSON. *S. Afr. med. J.*, **30,** 980–983. Oct. 13, 1956. 4 figs. 13 refs.

The author discusses this condition, as described by Craig and Landing (*Arch. Path.*, 1952, **54,** 321). The main characteristics are hepatomegaly, acholic stools, and in some instances a tendency to bleed. Generally the serum bilirubin level is raised and there is bilirubin in the urine. There is no Rh incompatibility. The liver is smooth, not nodular, and bile stained. The biliary tracts are always patent.

Microscopically the outstanding feature is the presence of numerous multinucleated giant parenchymal cells. These are up to 400 μ in diameter and contain as many as 20 nuclei.

Reference is made to the report of Dible *et al.* (*J. Path. Bact.*, 1954, **67,** 195), who presented 8 cases and considered that the condition was due to intra-uterine virus hepatitis, and to that of Smetana and Johnson (*Amer. J. Path.*, 1955, **31,** 747) who believed that it was due to failure of development of the intercellular bile canaliculi. It has been reported in siblings.

Evidence that the disease is due to a hepatotoxic virus is accumulating. Hepatitis virus A and virus B have been isolated, and it is thought that the path of infection is transplacental. Infants born of mothers who have infectious hepatitis during pregnancy do not contract the illness, probably because of the rapid development of antibodies in the mother.

L. J. Abramowitz

31. **ABO Incompatibility as a Cause of Hemolytic Disease of the Newborn.**

By I. DAVIDSOHN. *Obstet. Gynec.*, **8,** 318–322. Sept. 1956. 3 tables. 8 refs.

The author states that ABO incompatibility is responsible for haemolytic disease of the newborn approximately once in 3,000 pregnancies. Prenatal diagnosis is not possible but diagnosis can be made in the newborn although clinical signs of the disease are usually mild. In affected cases, anaemia is slight to moderate and jaundice may be present. Reticulocytosis and spherocytosis are pronounced. Fragility is increased. The Witebsky differential test gives a strong reaction in normal human serum, and a weak or negative reaction with a mixture of human serum with bovine albumin. (In Rh and other types of incompatibility the reaction is about equally strong in normal human serum and in the mixture.)

The prognosis in ABO disease is better than in haemolytic disease caused by Rh incompatibility. Exchange transfusion is necessary in only a few cases.

J. G. Dumoulin

32. **Erythroblastosis Fetalis: Review of Seventy-three Cases.**

By W. M. JACOBS and M. I. KOHN. *Obstet. Gynec.*, **8,** 131–134. Aug. 1956. 4 tables. 4 refs.

This report on 73 cases of erythroblastosis foetalis covers the years 1950–54 and comes from St. Joseph's Maternity Hospital, Houston, Texas. The incidence was 1 in 419 pregnancies, or 1 in 59 Rh-negative mothers, and these figures are lower than most reports of statistics for no very obvious reason. There were 35 foetal deaths. The view that erythroblastosis and prematurity together are very hazardous for the baby was borne out by this series.

Of the 73 patients, 60 were born alive and 38 ultimately survived. Of the 27 that had exchange transfusions, 23 survived. There were 17 deaths in the 33 cases who did not have exchange transfusion. Early exchange transfusion is the most potent weapon available today for the management of erythroblastosis.

J. G. Dumoulin

33. **Perinatal Infection and Perinatal Death.**

By J. A. M. SMITH, R. F. JENNISON and F. A. LANGLEY. *Lancet*, **2,** 903–906. Nov. 3, 1956. 11 tables. 4 refs.

The authors record the results of a trial designed to show what part infection plays in the causation of perinatal mortality and morbidity. The diagnosis of intrapartum infection and hence potential foetal infection was based on two criteria, viz., maternal pyrexia and foetal tachycardia. The prognosis for the infant was found to be worse if the maternal pyrexia lasted more than 48 hours. Notifiable puerperal pyrexia occurred more frequently in the untreated infected group than in the uninfected group. Inflammation of the placenta was three or four times as common in the untreated infected group as in the uninfected group. The authors considered that the bacteria reached the maternal decidua via the vagina and cervix. Infection spreads from here to the placenta or membranes or both. Sometimes it spreads to the foetus by the foetal blood stream or by aspiration of infected liquor. The bacteriological studies of the vaginal flora suggest that the antibiotic therapy of streptomycin and oxytetracycline reduces the incidence of potential pathogens and improves the prognosis for the foetus if it is possible to treat the mother for at least 48 hours before delivery.

H. H. Fouracre Barns

OBSTETRIC OPERATIONS

34. **Indications for Caesarean Section: A Consideration of Certain Aspects.**

By S. DEVENISH MEARES. *Med. J. Aust.*, **2,** July 14, 1956. 18 tables. 20 refs.

The subject is discussed against the background of the statistics at the Women's Hospital (Crown Street) from

1st July, 1949 to 30th June, 1954, during which time 22,981 infants were born. The Caesarean section rate was 1·4 per cent, 327 Caesarean sections being performed with no maternal deaths and a perinatal death rate of 8·5 per cent. Over eight years improved antenatal care led to a threefold decrease in the incidence of eclampsia, which was associated with a sixfold decrease in the number of Caesarean sections for pre-eclamptic toxaemia. The incidence in the latter half being 1 in 4,210.

The three commonest indications for Caesarean section were mechanical dystocia, uterine scar, and haemorrhage and these made up almost 70 per cent of the total. Over two-thirds of patients, who had undergone one previous Caesarean section, were delivered vaginally in the subsequent pregnancy.

In the whole series of 327 Caesarean sections there were 28 perinatal deaths three-quarters of which were associated with prematurity (birth weight under 5½ pounds). Of the perinatal deaths following Caesarean section for placenta praevia 80 per cent were associated with prematurity.

Patients whose pelves have a true conjugate of more than 8·4 cm. should be given an adequate trial of labour. In the trials lasting over 24 hours, the Caesarean section rate was 26·5 per cent. From the foetal point of view, prolonged labour (lasting over 48 hours) is to be feared, the perinatal mortality rate then being 10 per cent. Before Caesarean section is performed all patients should be examined radiologically to try to exclude foetal abnormality.

Author's Abstract

35. **Maternal and Fetal Mortality Associated with Cesarean Section.**

By L. T. HIBBARD and W. F. KROENER, JR. *West. J. Surg. Obstet. Gynec.*, **64**, 485–487. Sept. 1956.

The results are reviewed of 1,375 Caesarean sections at the Los Angeles County Hospital in the 5 years up to December, 1953. The incidence in the hospital was 3·11 per cent and about half the cases were repeat sections; disproportion and malpresentation accounted for 350 cases while placenta praevia and abruptio placentae occurred 169 times. There were 5 maternal deaths (0·36 per cent); 2 were unrelated to the operation, one being due to shock following uterine rupture and the other to (?) afibrinogenaemia. The other deaths were due to spinal anaesthesia, uncontrollable bleeding during a Norton extra-peritoneal operation and following abruptio placentae with massive uterine haemorrhages. There were 4 major post-operative complications, two following the Norton operation; since there were only 125 operations of this type in the series, the authors think that the technique should be used sparingly. There were 121 foetal deaths in the series (8·7 per cent) and the authors stress the fact that abdominal delivery does not of itself contribute greatly to this mortality; the risk to the baby comes from the obstetrical complication which necessitates operative delivery. More babies could be saved by better diagnosis, careful consideration of the optimum time for delivery, by appreciation of the hazards of haemorrhage, by the use of drugs which are effective in the problems of pregnancy and by less reliance on antibiotics to counteract the results of poor obstetrical judgment.

D. C. A. Bevis

MATERNAL MORTALITY

36. **Amniotic Embolism.** (L'embolie amniotique.)

By F. LEPAGE, L. LEMERRE and A. DUPAY. *Gynéc. Obstét.*, **55**, 45–63. 1956. 47 refs.

The authors, writing from Paris, state that they could only trace 55 true cases of amniotic embolism in the literature, and that most of these had been published in Great Britain or the United States. They discuss the aetiology, and the fatal forms, also those complicated by a haemorrhagic syndrome. They consider that for penetration of the amniotic fluid into the maternal circulation: (1) a force must be present to inject the amniotic fluid, (2) a tear in the membranes must occur, and (3) a deficiency must be present somewhere in the blood vessel walls.

The uterine contractions supply the force. The rent in the membranes is usually at the lower pole of the uterus; in two of the cases they describe a quantity of amniotic fluid remained in the uterine cavity. The breach in the vascular system can be either at the placental site or at the level of the endocervical veins. The writers state that there are three theories to explain the pathogenesis of amniotic embolism. First, the mechanical theory of Schneider, and they refer to his experimental work on rabbits. According to this, widespread pulmonary circulatory obstruction due to meconium emboli or other pre-formed debris is associated with shock and dilatation of the right heart. Secondly, there is the theory of anaphylactic shock associated with the names of Steiner and Lusbaugh, but this is not accepted by the authors. Thirdly, there is the thromboplastic theory of Weiner, Reid and Roby, which the authors consider helps to explain the haemorrhages associated with blood that fails to coagulate in these cases.

The prognosis is bad, and the maternal mortality is probably above 60 per cent. Two out of three infants will die either *in utero* or shortly after birth.

Treatment will depend whether these cases are seen in the phase of shock or haemorrhage. If in the first, oxygen, intravenous plasma or blood should be given, together with cardiovascular analeptics and atropine. Intubation and artificial respiration may be necessary. If seen in the haemorrhagic phase, intravenous fibrinogen 4–18 grammes will be required.

D. Maxwell

GYNAECOLOGY

37. **Pelvic Findings in the Elderly Institutionalized Female Patient.**

By C. E. FOLSOME, E. E. NAPP and A. TANZ. *J. Amer. med. Ass.*, **161**, 1447–1454. Aug. 11, 1956. 14 refs.

Female life expectancy has increased by 24 years in the United States since the turn of the century, and this has

increased the number of gynaecological geriatric problems. The authors have made gynaecological examinations in a group of 680 women between the ages of 41 and 111 years who required institutional care because of age, long-standing chronic disease or destitution. The cases were seen in the various municipal institutions in New York.

In review of the medical histories of these 680 cases it was observed that 228 had had prior major surgical or radiation treatment, and of these 175 were gynaecological operations. After pelvic examination the findings were classified into two main categories: (1) A fibrotic type (556 cases) and (2) An atrophic type (124 cases). All instances of carcinoma and prolapse occurred in the atrophic type. Cervical and vaginal smears were taken from all patients and four instances of cervical carcinoma were discovered. None of these patients had complained of a single symptom. In fact all of these elderly patients in the whole series exhibited a considerable "tolerance" to their symptoms, and many did not complain at all even in the presence of striking abnormalities.

The chief findings were 24 uterine fibroids, 5 ovarian tumours, 8 cases of leukoplakia of the vulva and one case of true kraurosis. There were 26 common lesions of the cervix, 51 cases of chronic cervicitis, 170 cases of relaxed anterior vaginal wall, 296 cases of rectocele, 61 cases of non-specific bacterial vaginitis and 86 cases of urethral caruncle. Also, 90 women had complete urinary incontinence and 29 women had definite stress incontinence. This survey emphasizes the need for improving the gynaecological care of an ageing population and especially in relation to nursing care and pelvic hygiene.

D. W. James

38. **Laurence-Moon-Bardet-Biedl Syndrome. A Family Group with Three Affected Siblings.**

By A. M. SIEGLER and E. WEISFOGEL. *Obstet. Gynec.*, **8**, 332–335. Sept. 1956. 1 fig. 12 refs.

The syndrome is diagnosed in patients who present the majority or all of the following deviations: obesity, hypogonadism, retinitis pigmentosa, mental deficiency and polydactylism.

The authors describe a family of 5 siblings, 3 of whom (1 man and 2 women) were affected. Their parents were consanguineous (first cousins).

J. G. Dumoulin

39. **Histochemical Observations on the Endometrium. II. Abnormal Endometrium.**

By D. G. MCKAY, A. T. HERTIG, W. BARDAWIL and J. T. VELARDO. *Obstet. Gynec.*, **8**, 140–156. Aug. 1956. 43 figs. 9 refs.

In this report are described histochemical changes in atrophic (post-menopausal) endometrium, cystic hyperplasia, adenomatous hyperplasia, carcinoma *in situ*, and adenocarcinoma of the endometrium.

In atrophic endometrium there is a general decrease in the histochemical constituents of the epithelial cells, the one exception being an increase in non-specific esterase activity. Cystic hyperplasia is the result of prolonged oestrogen stimulation and the histochemical reactions of the epithelium lining the glands are very variable: ribonucleoprotein may be abundant or undetectable. Alkaline and acid phosphatase activity is usually present. Glycogen is found in patchy distribution. Glycoprotein is abundant in the secretions. Non-specific esterase activity is seldom seen in the epithelium but is abundant in the macrophages. In adenomatous hyperplasia the same histochemical variations are found.

In carcinoma *in situ* ribonucleoprotein is scant in the cytoplasm of the epithelial cells. Alkaline phosphatase activity is not found while acid phosphatase activity is prominent. Glycogen and glycoprotein are present in small amounts and there is abundant non-specific esterase activity. This histochemical pattern more closely resembles progestational endometrium than proliferative endometrium. It is possible that some endocrine factor with an action similar to progesterone may be associated with cancer production.

The variability of histochemical reactions observed in benign abnormal endometria is found also in adenocarcinoma.

J. G. Dumoulin

40. **Postmenopausal Bleeding.**

By S. L. ISRAEL and L. L. WEBER. *West. J. Surg. Obstet. Gynec.*, **64**, 515–519. Sept. 1956. 12 refs.

In considering this symptom an arbitrary definition must be adopted as the menopause is frequently of indefinite establishment; the authors suggest that any resumption of genital bleeding after an interval of amenorrhoea of 1 year or more is significant. This bleeding must be regarded as uterine until proved otherwise and must be viewed with suspicion until a definite diagnosis has been established by careful examination, uterine curettage, biopsy of the cervix and further observation of the patient. Twenty years ago it was averred that 65 per cent of patients with the symptom had a malignant lesion, nearly always of the corpus uteri; as increasing numbers of post-menopausal women are admitted to hospital solely for diagnostic procedures, more benign conditions are found, resulting in a relative lowering of the incidence of carcinoma (variously reported as between 27–37 per cent). A negative curettage automatically places the patient in the benign category, but the follow-up of such patients cannot be overemphasized. Diagnostic pitfalls include oestrogen withdrawal bleeding, atrophic vaginitis and cervical polyposis; careful follow-up is essential. The post-menopausal uterus is very thin-walled and especially liable to perforation at curettage; it is also liable to damage from intracavitary radium; as a result of this, if bleeding recurs the treatment of choice is abdominal hysterectomy with bilateral salpingo-oöphorectomy.

D. C. A. Bevis

41. **Cervical Mucus Arborization Aid in Ovulation Time.**

By I. FORMAN. *Obstet. Gynec.*, **8**, 287–292. Sept. 1956. 9 figs. 4 refs.

Cervical mucus arborization is a simple test of oestrogen activity. The test is negative in the post-menstrual phase because of inadequate oestrogen effect. Arborization becomes increasingly evident as ovulation

approaches and the oestrogen level rises. The test becomes negative in the pre-menstrual phase because of the inhibiting action of progesterone so that examination of cervical mucus at midcycle and in the pre-menstrual phase is a fairly accurate test for ovulation. Daily examination of cervical mucus in the pre-ovulatory phase is a distinct aid in ovulation timing.

J. G. Dumoulin

42. **The Respective Roles of Hormonal Imbalance and Infection in the Aetiology of Female Sterility.** (Parts respectives de l'origine hormonal et de l'origine infectieuse des stérilités féminines.)

By C. Beclaire. *Gynéc. prat.*, **7**, 168–186. 1956. 21 refs.

The hormonal control of the female genital organs has been studied in great detail in the past years, and some authors do not hesitate to put hormonal imbalance at the head of the list of causes of female infertility. In reality, infertility in women is due to causes which fall into two main groups—infection and hormonal imbalance. The relative importance of these two groups must be assessed. Statistics collected by the author over the past thirty years show that although hormonal imbalance is an important cause of infertility, especially primary infertility, the role of infection is of much greater importance. Statistics produced in 1937 resemble very closely the series of cases analyzed in 1952. Of cases of primary infertility, 23 per cent showed hormonal imbalance (the author includes congenital maldevelopment in this category). Sixty-five per cent showed evidence of infection which was gonococcal in half the cases (the figures for 1952 are 38 per cent hormonal or developmental and 57 per cent infective). In the case of secondary infertility, the corresponding figures are 3 per cent and 91 per cent in 1937, and 22 per cent and 81 per cent in 1952. Of particular interest are the percentages of cases showing normal tubal patency in the 1952 series. Of patients attending for primary infertility, only 28 per cent had patent tubes as against 35 per cent of those with secondary infertility. *Geoffrey Dixon*

43. **The "Thirteenth Day" Test.** (Le test du "treizième jour".)

By J. Séguy. *Gynéc. prat.*, **7**, 137–143. 1956. 20 refs.

This test, described by the author in 1931, consists of the examination of the cervical mucus some twenty hours after intercourse on the thirteenth day of the cycle. This enables an assessment to be made not only of the quality of the spermatozoa and the mucus, but also of their compatibility. When there appears to be an otherwise unexplained incompatibility, the author carries out *in vitro* tests using donor spermatozoa against the cervical mucus under investigation and vice versa.

Geoffrey Dixon

INFECTIONS

44. **Gynaecological Treatment of Septicaemia due to Clostridium welchii (A Critical Study of 38 Cases of Post-abortive Anuria).** (Conduite à tenir du gynécologue devant une septicémie à perfringens. Etude critique de 38 cas d'anurie post-abortive.)

By —. Seguy and —. Henrion. *Gynaec. et Obstet.*, **55**, 64–74. 1956.

The authors of this report from Paris state that many of their cases did not come under their care until 3 or 4 days after admission. As a result the general condition of the patients was often alarming, and their blood urea levels were often high. In their early experiences of these cases their main aim was to determine whether or not there was evidence of infarction of the uterus. If so, in their opinion operation was indicated, but in fact they found this lesion to be extremely rare. In this series the mortality was high, 16 patients dying out of 38.

They divide their cases into three main groups: First, those in which there is purely and simply a *Clostridium welchii* septicaemia, and the local conditions in the uterus are being satisfactorily overcome. In these cases the clinical picture is that of a young woman who has had some uterine interference and who some hours later shows signs of septicaemia with rigors, high temperature, vaginal bleeding, frequent vomiting and lumbar pain. Jaundice quickly develops, with oliguria or anuria. There is a gross secondary anaemia with rapid rise in the blood urea. The abdomen is soft and not distended, the body of the uterus is enlarged but not painful when moved. Under such circumstances the writers advise: (1) large doses of penicillin, but not sulpha drugs or terramycin as both these may worsen the blood urea level. (2) If the uterus has not been emptied, complete removal of the contents using the finger, ovum forceps, and occasionally a blunt curette, after dilatation if that is necessary. It is essential to ensure that any organized blood clots and decidual debris which may have escaped even an experienced operator are completely removed. A light gauze pack soaked in penicillin and streptomycin is then inserted for 24 hours.

The second group concerns cases in which the picture of *Cl. welchii* septicaemia is incomplete, and the differential diagnosis includes cases of: (*a*) jaundice when anuria, at any rate at the onset, is not present, (*b*) oliguria when *Cl. welchii* is not the cause, and (*c*) post-transfusion anuria in a woman who has had uterine interference.

The third group concerns cases in which surgical abdominal operation and possibly hysterectomy is required. The indications are: (*a*) abdominal rigidity, (*b*) abdominal distension and meteorism, (*c*) a soft subinvoluted, often retroverted uterus, which is tender on being moved, and (*d*) persisting pyrexia, deepening jaundice, rising blood urea, dyspnoea, general collapse and increasing leucocytosis.

[The writers do not allude in detail to the actual treatment of the anuria except by peritoneal dialysis. There is no mention of peanut oil by indwelling polythene tube.]

D. Maxwell

45. **Streptomycin in Advanced Pelvic Tuberculosis.**

By M. L. Bobrow, L. B. Winkelstein and S. Friedman. *Obstet. Gynec.*, **8**, 299–307. Sept. 1956. 6 figs. 1 table. 19 refs.

The authors present 6 cases of advanced pelvic tuberculosis showing well-defined gross and microscopic

pathology. Two followed normal full-term deliveries. Gross pathology with pelvic masses, induration, and progressive pelvic peritonitis, produced by tuberculosis is neither resolved nor controlled by streptomycin and P.A.S.

The anti-tuberculous drugs may heal endometrial and cervical tuberculosis despite the presence of other pelvic tuberculosis. However, healing of such lesions must not be interpreted as a sign of healing of the tubes and ovaries.

The immediate results of surgical intervention are excellent. Surgical patients make quick and uneventful returns to good health, free of pelvic complaints. Eradication of the local infection enhances healing of systemic tuberculosis by lessening the drain on the body's protective forces. Anti-tuberculous drugs are useful in the pre- and post-operative treatment.

J. G. Dumoulin

NEW GROWTHS OF THE REPRODUCTIVE ORGANS

46. **Registration of Female Genital Cancer in Australia.** By K. A. McGarrity. *Med. J. Aust.*, **1**, 641–644. Apr. 21, 1956. 5 figs.

This paper was read at a General Meeting of the New South Wales Fellows and Members of the Royal College of Obstetricians and Gynaecologists held on 25th May, 1955. McGarrity pointed out the need for mobilization of statistics relating to genital cancer and explained the purposes of the Registry as follows:

(1) To establish a uniform method of recording throughout Australia.
(2) To provide a system from which research workers could make surveys of statistical data.
(3) To provide facilities in a central office to supply information on the effects of treatment.

In summing up the systems of history-taking, collection of statistics, and follow-up which prevail in Australia, Dr. McGarrity said that even the best of these systems depended upon a history taken by a junior member of the medical profession. A Registry could only exist on absolutely correct information. The system in many hospitals was inadequate for recording anything except a few basic details about each patient. Therefore, principles that had to be established for the Registry were:

(1) To use a form that would provide the least possibility of inaccurate information—to do this it was found necessary to have fixed answers. The information collected from these fixed answers could be placed on to a Hollerith punch card. The form had been designed also to operate and act as a history sheet which could replace the history sheets in hospitals for recording information relating to genital cancer, and already it had been adopted at the Women's Hospital, Crown Street, Sydney, where the Superintendent found its use had greatly improved the standard of clinical histories.

(2) To provide a system that is uniform and national, in order to avoid the danger of selection of cases that would occur with local statistics gained from either individual hospitals or even States. This meant that the system should be controlled by the Regional Council of the College, rather than by a local body, so that it could grow uniformly throughout Australia.

(3) The basic form will always be retained at the Central Registry and the information placed on it will be supervised by a senior member of the gynaecological staff, who, in most cases, will be a member of the College. In this way, information obtained will be as accurate as possible. This is in contrast to most other forms of registration that depend on an abstract card, when the worker who requires further information must go back to the original histories.

The mechanics of this scheme will be to collect information on a state basis by a State Registry, which will forward its histories to a Central Australian Registry which will be responsible for putting the information on to a Hollerith punch card. In order to gain this information, the hospital or private doctor should fill in a form, a registration card, and a follow-up card, for each case of genital cancer. The registration card should be submitted immediately the provisional diagnosis of malignancy is made. Later the form and follow-up card should be submitted to the Central Registry when the first treatment has been concluded. Each hospital keeps an admission and discharge sheet to list its registrations of such patients. When the form reaches the Central Registry, the information from the fixed questions is extracted on to the Hollerith punch card. Here, a group of College members will assess each case from the point of view of diagnosis and staging, so that every aspect of information put on the punch card will be as correct as possible.

In this way, in a short time, with the amount of information that should come in, properly tabulated, it should be possible to find out the answer to many controversial problems by submitting the punch cards to analytical machine sorting. Dr. McGarrity said there were any number of possible combinations of clinical and pathological findings that could be associated in this way. Similarly, the type of treatment and its effect could be assessed quickly and accurately by the same method of machine sorting, the master-card giving the operator directions as to how to extract the information required during this process. In this way, information regarding malignant disease would be controlled, and a follow-up system would be established for every patient reporting with malignant disease. He concluded by saying that the establishment of this system throughout Australia would not be very costly or very arduous, and if every doctor or hospital would co-operate, the project which promised so much could easily be carried out. The meeting, after discussion, agreed to establish the Registry from 1st July, 1955.

S. Devenish Meares

47. **Transtubal Spread of Tumor Cells in Carcinoma of the Body of the Uterus.** By T. Dahle. *Surg. Gynec. Obstet.*, **103**, 332–336. Sept. 1956. 2 figs. 14 refs.

This is an excellent study from the Norwegian Radium Hospital, Oslo, of the frequency of transtubal spread to

the peritoneal cavity of malignant cells from carcinoma of the body of the uterus.

Twenty-one cases of carcinoma corporis were treated by total hysterectomy and bilateral salpingo-oöphorectomy. In 20 cases the surgical specimen showed adenocarcinoma, in 1 case there was an adenocarcinoma with squamous metaplasia. In no case was there penetration of the tumour to the peritoneal surface of the uterus but in 1 case there were metastases in 1 tube and both ovaries. In no case was there bilateral occlusion of the Fallopian tubes, but in 6 cases there was unilateral occlusion.

Wash smears and direct smears from the tubes and wash smears from the pouch of Douglas were prepared in all cases. Twenty ml. of physiological saline solution was used for the latter. Before performing the hysterectomy the tubes were removed and the washing and the tubes were immediately sent for cytological examination.

By cytological examination tumour cells were observed from 1 or both tubes in 11 patients (6 unilateral and 5 bilateral cases) and from the pouch of Douglas in 7 patients. In 6 cases with positive smears from the Douglas cul-de-sac, tumour cells were also observed in 1 or both tubes.

When tumour cells are seen in the pouch of Douglas it may be assumed that they may also spread to other parts of the peritoneal cavity. It is not known if these cells are viable but they must be regarded as a possible aetiological factor in the development of metastases. In an attempt to destroy them, during the past year the author has given a prophylactic radiogold treatment to 9 patients operated upon for carcinoma of the body of the uterus. Before closing the abdomen the peritoneal cavity was filled with 1½ litres of saline solution and on completion of the operation about 100 millicuries of radioactive colloidal gold was introduced through a catheter into the artificial abdominal fluid. In addition all patients were given post-operative radiotherapy.

While no harmful effects have been observed it is not possible at the present time to say anything conclusive about the results of this therapy.

John P. Erskine

48. **Scattered Thoughts on Cancer of the Uterine Cervix.**

By J. T. Louw. *S. Afr. med. J.*, **30**, 933–937. Sept. 29, 1956. 7 tables. 3 figs.

Although innumerable papers have been written on this subject, the author stresses the importance of their publication, for it shows that active thought and endeavour are constantly being hurled at cancer.

Three clinics: (*a*) cervical erosion, (*b*) vaginal discharge and (*c*) an endocrine clinic, each with its own team, have been established in the Cape Town unit. Centrally, a watch is kept on their patients in order to assess whether certain conditions predispose more than others towards cancer of the cervix.

Cytological studies in 821 cases from the erosion clinic revealed positive smears in 38 cases. Nine of these were confirmed histologically, 5 showed no histological evidence of cancer and 24 are being followed up. Of 654 negative slides, 1 cancer was proved histologically. Of 119 doubtful cases, 62 repeat smears were negative and in 57 there was sufficient doubt to warrant histology.

No treatment is carried out without histological confirmation, and every patient with a suspicious erosion, a positive or doubtful smear is admitted for thorough biopsy under general anaesthesia. A case of carcinoma *in situ* is mentioned in which the entire cancerous area had been removed by cone biopsy.

A comparison between the racial groups reveals interesting features:

(*a*) Whereas in the whites cancer of the breast is more frequent than cancer of the cervix, this is not so in the coloured population.

(*b*) The ratio of the incidence of cancer of the cervix to that of cancer of the body of the uterus is 2 : 1 in whites and 10 : 1 in coloured.

(*c*) The majority of cases of cancer of the cervix occur at an earlier age in the coloured than in the white.

(*d*) The habits of sexual intercourse in coloured patients with cancer of the cervix revealed a higher incidence of intercourse before 20 years, a slightly increased incidence of frequency of intercourse, and a very much higher incidence of extra-marital relationships.

The author states that cervical cancer may yet prove to be a virus disease transmitted by sexual intercourse. An interesting case of a clean, circumcised Malay man is mentioned. Both his wives developed cancer of the cervix.

With regard to treatment, two months after radiotherapy (generally the Stockholm method) patients are re-assessed with a view to surgery. Pre-operative investigation and treatment must be thorough and complete. The nature of the operation can only be determined after the abdomen is opened. Often 2 teams work simultaneously, e.g., when abdomino-perineal resections are done. Great attention is paid to preserving blood supply when possible. A method of dealing with the ureters in anterior exenteration is described and urinary difficulties following posterior exenteration are discussed.

Operative results are tabulated. In 100 major operations for carcinoma of the cervix there were 7 post-operative deaths in the first month, 4 ureteric and 2 vesico-vaginal fistulae. In 81 cases of radical hysterectomy only 1 patient died. There were no deaths in 22 cases requiring major surgery for cancer of the body of the uterus, the vagina or the rectum.

These patients are an unselected group. The author feels that staging carries too many variables and that its part in the evolution of the study of cervical cancer has been played.

L. J. Abramowitz

49. **Experimental Ovarian Tumours.** (Experimentelle Ovarialtumoren.)

By E. Fels. *Arch. Gynäk.*, **188**, 63–76, 1956. 12 figs. 33 refs.

After discussing the various methods of producing ovarian tumours in laboratory animals, with special reference to breed, success rate and time interval between

induction and development, Professor Fels deals with his own experiments. These comprised 2 different means of tumour production in rats: (*a*) implantation of one ovary into spleen, liver or kidney, and (*b*) ligation of the ovaries. The time interval between implantation and tumour development varied from 177 to 625 days and the sex of the receiving animal did not seem to be of importance. The time interval between ligation and tumour formation was even longer, varying between 228 and 691 days. The sequelae of ligation were persistent oestrus, uterine hypertrophy, endometrial hyperplasia and sometimes epithelial metaplasia. The author ascribed these sequelae to a hyperfunction of the pituitary and he, therefore, tried to stimulate the pituitary further by exposing the experimental animals to a continuous light influence. This increased the tumour production rate from 38·9 per cent (ligation alone) to 58·5 per cent (ligation plus light exposure). Exposure to light alone was not tumour producing.

The histological structure of the tumours was independent of their aetiology. The following histological types were encountered: luteomas, granulosa cell tumours, tubular adenomas and thecomas; frequently a combination of 2 or more cell types were present in the same tumour. In a total of 130 experimentally induced tumours 7 were malignant, 5 being carcinomatous and 2 sarcomatous growths, and 3 had metastasized. These tumours produced an excess of oestrogenic but no androgenic hormones, but despite the excess oestrogens only 28 per cent of the experimental animals with successful tumour take showed castration pituitaries. Transplantation of experimentally induced tumours into the spleen of other, previously castrated, rats was possible in 11 out of 22 rats with persistence of hormonal activity. A change in the histological appearance of the transplants was occasionally noted.

Professor Fels concluded from these experiments that the increase in gonadotrophic activity of the pituitary leading to increased ovarian stimulation was primarily responsible for tumour production.

Erica Wachtel

50. **A Description of Metastatic Tumours of the Ovary: Krukenberg Tumours. (A Pathologico-Anatomical Study of 9 Cases.)** (Particolarita sui tumori metastatici dell'ovaio: i tumori di Krukenberg. Rilievi anatomo-patologici su 9 casi.)

By A. Fabiano, F. Ferraris and G. Bongiovanni. *Ann. Ostet. Ginec.*, 77, 1121–1144. Dec. 1955. 12 figs. 80 refs.

This illustrated description of nine Krukenberg tumours includes a review of the extensive literature on the subject. Details of these cases are as follows:

Case 1. Tumours secondary to massive carcinoma of stomach; the ovaries were massive and entirely replaced by neoplastic tissue. On histological examination this showed a pseudo-glandular picture with hypersecretion. Signet ring cells were present in the glandular lumina.

Case 2. Tumours secondary to scirrhus carcinoma of the stomach with glandular metastasis. The ovaries were made up of metastatic tissue, enclosed in a fibrous capsule. This epithelium consisted of nests of epithelium. The epithelium was of the cylindro-mucous type. Pseudo-tubules and pseudo-glands were numerous. Signet ring cells were numerous. There was considerable stromal reaction, strands of fibrous tissue separating the glandular elements.

Case 3. Tumours secondary to carcinoma of the colon, with peritoneal spread and massive secondaries in both ovaries. Histological examination revealed that the mass of the tumours was made up of numerous fusiform connective tissue fibres. At the periphery these were condensed to form a capsule. In the centre, the fibres were to form alveolar spaces. Mucus-secreting cells were disseminated throughout the parenchyma of the tumour. In the greater part of the glandular element, there were some very large cells laden with mucus. Some of these had central nuclei, while in others the nuclei were eccentric.

Case 4. Tumours secondary to carcinoma of the stomach. The histological picture of the ovaries revealed diffuse infiltration with columns of epithelial cells; this often assumed an alveolar appearance and the cells showed mucous vacuolization typical of Krukenberg's tumour.

Case 5. Carcinoma of the pancreas with massive secondaries in the peritoneum, liver, spleen and ovaries. The ovaries showed that the original structure was replaced by pseudo-tubular malignant tissue. The epithelial cells were typical of those of mucus secreting glands. There was a marked stromal reaction.

Case 6. Gastrectomy was performed for carcinoma of the pylorus. Later large ovarian tumours were removed. On section, these presented an atypical picture, containing trabeculated fibrous tissue enclosing glandular elements. The glands showed some tubule formation and the cells contained mucoid secretion.

Case 7. A laparotomy was performed for a large pelvic mass. This proved to be ovarian tumours, adherent to colon, appendix and mesentery. Histological examination revealed a pseudo-glandular picture with considerable fibrous tissue reaction. The cells contained mucoid droplets, giving the typical "Signet ring" appearance. No indication is given as to the probable site of a primary tumour.

Case 8. Carcinoma of the stomach with metastases in the peritoneum, anterior mediastinum, heart diaphragm, liver, pancreas, abdominal lymph glands and ovaries. Histological examination of the ovaries revealed some normal structure, including a Graafian follicle, a corpus albicans and a follicular cyst. Most of the ovary, however, consisted of fibrous connective tissue, with large, delicate strands of pre-collagenous fibres. Among the fibres were pseudo-glandular formations. Many of the epithelial cells presented a semilunar appearance owing to the presence of mucoid droplets. Myxomatous degeneration was apparent in some of the strands of fibrous tissue.

Case 9. Carcinoma of the stomach, treated by gastrectomy. At autopsy there was peritoneal carcinomatosis with abundant free fluid. Both ovaries were replaced by solid tumours. Histological examination of the ovaries revealed nests of epithelial cells with intense

stromal reaction. The epithelial cells tended to form pseudo-glands, and were mucoid in character. The mucicarmine reaction showed up the "Signet ring" shape.

These cases are discussed in the general light of metastases of malignant tissues. Neoplastic elements from the upper alimentary tract or the breasts may reach the ovary by metastasis (cellular embolism in lymphatics or blood vessels), by permeation (nests of neoplastic cells which insinuate themselves into the lymphatics) or by peritoneal dissemination (by cells falling free in the peritoneal cavity). These various possibilities are fully discussed in relation to the known methods of spread of malignant disease. Implantation of ovarian metastases and ectopic endometriosis may have a similar origin. Metastatic emboli cause intense reactivation of connective tissue, which may be regarded as to some extent a defence mechanism against further spread of the disease.

Josephine Barnes

51. **Further Observations on Ectopic Endometrium of the Fallopian Tube.**

By I. C. RUBIN, L. R. LISA and S. TRINIDAD. *Surg. Gynec. Obstet.*, **103**, 469–474. Oct. 1956. 6 figs. 16 refs.

This is a study from the Doctors Hospital, New York, of the incidence and clinical importance of endometrium in the lumen of the extra-uterine portion of the Fallopian tube. Three hundred and thirty-five tubes from 200 uteri removed surgically were examined. The tubes were cut in serial blocks 3 mm. thick and slides were prepared from each block. The ages of the patients from whom the uteri were removed ranged from 23 to 71 years with the majority falling in the 5th decade.

Endometrium was present in the lumen of the extra-uterine portion of the Fallopian tube in 19 of the 200 specimens, an incidence of 9·5 per cent. The endometrium was represented by glands and stroma in 14 cases and by endometrial stroma and surface epithelium of uterine character, either alone or combined, in 5 cases. In 13 cases in which both tubes were available for study, endometrium was found on both sides in 3. The location of the endometrium varied considerably but the isthmic segment was most frequently affected. The gross anatomy of the tube was normal in the specimens in which the endometrium was limited to the mucosa but distortion similar to salpingitis isthmica nodosum was present where the endometrium had penetrated into the muscular wall.

Endometrium in the extra-uterine portion of the tube was usually, but not invariably, associated with the presence of endometrium in the interstitial segment. Twenty-six uteri showing unilateral or bilateral endometrium in the interstitial segment were free from extra-uterine tubal endometrium. Cyclic changes in the tubal endometrium were lacking.

Of the 19 patients with isthmic or ampullary endometrium 6 had had endometriosis of the ovaries or pelvic peritoneum and 12 had uterine adenomyosis. Of the other 181 patients, 91 had uterine adenomyosis and 16 had endometriosis of the ovaries or peritoneum. The histogenesis of endometrium occurring within the lumen of the Fallopian tube is discussed and it is considered probable that it rests on a developmental basis. Tubal adenomyosis does not appear to have any relation to antecedent salpingitis and, although placental implantation may occur in tubal endometrium, its presence does not seem to play a predominant role in tubal pregnancy. However, tubal adenomyosis may be a significant factor in some cases of sterility.

The authors recommend the following clarification in the terminology—"ectopic tubal endometrium" to designate the presence of endometrium confined to the mucosa, "tubal adenomyosis" to designate penetration into the tubal muscular walls and "tubal endometriosis" to designate serosal involvement.

John P. Erskine

OPERATIONS

52. **Evaluation of Pelvic Exenteration for Advanced Cancer of the Cervix.**

By A. BRUNSCHWIG and W. DANIEL. *Surg. Gynec. Obstet.*, **103**, 337–341. Sept. 1956. 8 figs. 5 refs.

This is a progress report from the Memorial Center for Cancer and Allied Diseases, New York. The results in cases of carcinoma of the cervix only are considered. In the majority of instances the patients presented recurrent cancer, failures of previous treatment.

Of the 336 cases of carcinoma of the cervix in which either complete or anterior pelvic exenteration was performed, 93 or 27 per cent were fresh cases. Most of these were classified as Stage 3 or Stage 4. In the past 2–3 years more anterior exenterations have been performed for Stage 2 cases in the presence of actual parametrial involvement and encroachment on the bladder or ureter.

The authors do not now attempt exenteration unless previous laparotomy indicates that all macroscopic evidence of disease can be removed. Other important factors to consider in operating upon patients by this type of surgery are the general medical condition of the patient, location of home and mental status of the patient.

The surgical mortality for the overall group was 16 per cent. Since 1950 the mortality in 86 consecutive anterior exenterations was about 6 per cent. The chief cause of death, despite advances in blood transfusion therapy, has been surgical shock.

The most significant finding in the pathological study has been the presence or absence of pelvic node metastases. Of 100 cases of pelvic exenteration performed 5 or more years, 12 of 67 patients (18 per cent) are living who had negative lymph nodes. In the positive node group there has been only one 5 year survivor.

One hundred and eleven patients have been followed 5 or more years and the 15 per cent survival obtained certainly compares favourably with the results obtained in treating advanced carcinoma of the oesophagus, lung, stomach and pancreas.

The various methods of urinary tract diversion are discussed very briefly.

The authors conclude that exenteration operations

would now seem to be established procedures capable of offering benefit to patients with advanced pelvic cancer, including especially those with recurrences following failure of radiation or more conservative forms of surgery.

John P. Erskine

53. **Postoperative Results of Total Hysterectomy With and Without Oophorectomy.** (Ein Beitrag zum Studium des postoperativen Zustandes nach Totalexstirpation des Uterus mit und ohne Adnexen.)

By R. PREISIG. *Gynaecologia, Basel*, **142**, 269–278. Oct. 1956. 5 tables. 10 refs.

The author attempted to follow up all cases of hysterectomy for benign lesions, performed at the Kantonspitals Winterthur between 1942–52. There were 170 patients of whom 127 (74 per cent) were examined and questioned—8 of these were eliminated because of hormone treatment, leaving 119. Of these 34 had 1 ovary removed, 54 both.

At a personal interview questions were asked concerning scar pain, joint pain, digestive upsets, circulatory complaints such as flushings, giddiness and anginal attacks, loss of libido, vaginal discharge and any psychological changes such as moodiness, depression or insomnia. The final question was, did the patient consider the operation a success. The patients were typed according to Kretchmer's classification, and their general appearance noted. The scar and skin were examined, hair growth noted, joint movements, urinary and digestive systems tested and the heart and blood pressure. Finally a bimanual vaginal examination was done and a speculum inserted.

The findings varied with the length of time postoperatively and therefore the patients were divided into 3 groups, (1) 1–2 years post-operation, (2) 3–5 years, (3) 6–10 years. Under each group tables set out the findings in 3 columns according to the operation, (1) hysterectomy only, (2) 1 ovary removed, (3) both ovaries removed.

The operation results were good, only one patient complained of stress incontinence and 3 had a slight cystocele. Ninety-four were married, 6 complained of slight dyspareunia but 35 had not had intercourse since the operation.

All symptoms were most pronounced in the group with bilateral oöphorectomy, but varied in intensity and prolongation. Half the patients in this group were dissatisfied with the operation 10 years afterwards.

The author concludes that ovarian hormonal withdrawal is most pronounced 2–4 weeks post-operatively, shown mainly by flushings and perspiration. He states however that they and later symptoms such as gain in weight and vaginal discharge can be controlled satisfactorily by hormone therapy. The psychological changes did not correspond so closely to the type of operation, and although admitting that the numbers were too small to be conclusive, he considers depression largely due to the patient's lack of fertility, and depended mainly on their Kretchmer build, the "leptosome" type becoming readily depressed and the "pyknisch" complaining of loss of libido and a tendency towards hirsutism.

[Unfortunately symptoms are not related to the age of the patient at the time of operation. The author gives no details of his hormonal therapy.]

Jean Hallum

54. **Treatment of Tubal Sterility by Linear Salpingotomy.** (Le traitement de la stérilité tubaire par la salpingotomie linéaire.)

By A. CHALIER. *Gynéc. prat.*, **7**, 129–136. 1956. 3 figs. 1 ref.

The author describes an operation for the relief of obstruction in the distal part of the tube which differs from the more commonly practised salpingostomy, in that the greatest possible length of tube is opened in the hopes of diminishing the possibility of subsequent closure. After opening the abdomen, the affected tube is freed from adhesions and the fimbriated end located. In so far as possible, the fimbriae are then opened out and a sound passed into the ostium. With fine scissors, the tube is then opened along its upper surface as far as the uterus. Haemostasis is secured by the individual ligation of each bleeding point. If the tube shows any tendency to curl up, the two edges are stitched back to the broad ligament. Seventy-one operations were performed before 1954. Of these eleven (15·5 per cent) became pregnant. Ninety-eight cases have been dealt with in this way since then, but the results are not yet known. The author feels that even when not followed by successful pregnancy, the operation serves a useful purpose as it brings about a cure of the salpingitis which has produced the tubal damage.

Geoffrey Dixon

55. **Dipipanone Hydrochloride in the Treatment of Severe Pain.**

By R. O. GILLHESPY, E. COPE and P. O. JONES. *Brit. med. J.*, **2**, 1094–1095. Nov. 10, 1956. 5 tables. 4 refs.

This article records the result of administering a new analgesic, dipipanone hydrochloride ("Pipadone") to 100 medical cases and 100 patients who had had gynaecological operations.

Patients in the latter group were given subcutaneous injections of 25 mg. six-hourly following operation, and in 95 per cent of cases there was complete relief from pain. Moderate relief was obtained in 4 per cent of patients and only slight relief in one case. The onset of analgesia occurred within 10 minutes and maximal relief was obtained in about 20 minutes. The effect lasted 5–6 hours.

Dipipanone hydrochloride seemed to be more effective than analgesics such as morphine, omnopon and pethidine, and side effects were rare though slight nausea, vomiting, giddiness and vomiting were noted at times.

The drug seemed to have but little hypnotic effect and patients were completely co-operative. Early leg and breathing exercises were facilitated. No obvious respiratory depression or change in blood pressure or pulse rate occurred and the blood picture was not altered. There were no complaints of anorexia or constipation. No conclusion regarding habit formation could be drawn.

R. W. Grayburn

UROLOGY

56. **The Female Urethra: Observations on the Anatomy, Pathology, and Treatment of its Occlusion Mechanism.** (Die weibliche Urethra, funktionelle Anatomie, Pathologie und Therapie des Verschlussmechanismus.)

By W. LANGREDER. *Zbl. Gynäk.*, **78**, 561–609. Apr. 14, 1956. 43 figs. 209 refs.

In order to investigate "functional incontinence" (excluding neurological disorders) the author studied anatomical sections through the urethra and adjacent tissues. Continence depends on both urethral and para-urethral structures. The various occlusive mechanisms are described in detail:

(1) *The urethral epithelium* itself plays an important role. It has thick folds, which are largest in adult women, and smaller in children and the aged. Cyclical changes occur in the epithelium. During the follicular phase of the menstrual cycle there is desquamation; in the progesterone phase the epithelium becomes thicker with elongated cells. The cells are scanty post-partum and after the menopause. Oestrogens cause epithelial proliferation and also improve the tone of the urethral muscle.

(2) *The subepithelial tissues.* In the proximal urethra there is a complex venous plexus. Congestion of this plexus varies during the phases of the menstrual cycle. The blood flow is augmented by oestrogens.

(3) *The urethral smooth muscle* is the most powerful agent in occlusion of the urethra. The muscle fibres are arranged spirally, enclosing the whole urethra. At the upper end they are continuous with the muscle of the bladder. Outside the spiral layer there are longitudinal muscle fibres, also continuous with those of the bladder. Occlusion of the urethra is effected by contractions of these muscles and those of the bladder base. The muscle is more contractile in the follicular phase of the menstrual cycle, and less active in the secretory phase. Peri-urethral fixation is an important factor in facilitating the action of these muscles.

Apart from these structures in the wall of the urethra many para-urethral structures are concerned in the control of micturition.

(4) *The levator ani muscle and its pelvic fascia.* In young women the pubo-coccygeus is directly related to the urethral muscle wall, and the urethral fascia blends with the fascia of levator ani. Contraction of the levator directly compresses the urethra. Strengthening the levator by remedial exercises, and the use of the "perineometer", may help cases of incontinence. Operative elevation of the pelvic diaphragm may have a direct curative effect.

(5) *The deep transverse perineal muscle* is described as the external sphincter of the urethra, but weakness of this muscle is a rare cause of incontinence unless the levator is also inefficient. Exercises may improve the tone of this muscle. For operative repair of the muscle an incision is made at the side of the vagina as far as the urethral orifice so as to expose the posterior and lateral walls of the urethra; the muscle can then be approximated behind it.

(6) *The bulbo-cavernosus muscle* compresses the distal urethra. The corpora cavernosa and various para-urethral fixing tissues lie between the bulbo-cavernosus and the urethra itself. Interposition operations on this muscle are sometimes practised (Martius).

(7) *Fixation to the symphysis.* The urethra is very firmly fixed to the back of the symphysis pubis, through the strong urethro-pubic fascia. The bladder is also fixed to the symphysis by fascial attachments. In cases of prolapse the upper urethra is detached from the symphysis. Operations such as those of Marshall and Marchetti are designed to fix the bladder base and urethra to the symphysis. The cave of Retzius contains a fine mesh of elastic and muscular fibres, continuous with those of the pubo-vesical or pubo-cervical ligaments.

(8) *Fixation to the vulva.* The urethra is fixed to the vulva by interlacing fascial fibres, continuous with the erectile tissue of the corpora cavernosa and the fascia of bulbo-cavernosus. Attempts have been made to treat incontinence by advancing the urethra and attaching it to the clitoris.

(9) *Attachment to the vagina.* The urethra appears to lie in the vaginal wall in its lowest third. The tissue which binds the urethra to the vagina and to tissues lateral to it is often described as fascia, but in fact consists of smooth muscle. This attachment between the lower part of the urethra and the vaginal wall may be described as the "urethro-vaginal sphincter". After childbirth this urethro-vaginal attachment may become slack.

During pregnancy the vagina increases in both width and length. These changes facilitate the passage of the child but lead to a looseness of the vaginal wall in the region of the urethra which is most evident in the puerperium, when the vaginal introitus gapes and its wall is slack, giving the appearance of a urethro-cystocele. Epithelial proliferation occurs and this, combined with weakness of the fixing structures of the vagina, predisposes to incontinence of urine later in life. Tightening of the vaginal wall at colporrhaphy, combined with shortening of the urethro-vaginal fascia, is an important part of treatment, and various techniques are described.

(10) *Fixation to the paravaginal tissues.* Above the attachment of the urethra to the anterior vaginal wall there is a large sheet of tissue consisting of smooth muscle which runs laterally and fixes the vagina to the pelvic wall.

(11) *Fixation to the parametrium.* Relatively strong fascial strands run from the bladder neck to the ventral parametrium. This vesico-uterine ligament has a powerful effect in elevating the base and neck of the bladder. In severe degrees of prolapse fixation of the lateral urethro-parametrial tissues, as described by Donald and Fothergill, is essential. Suture of the para-urethral and parametrial tissues raises the uterus above the level of levator ani and also elevates the vaginal wall and urethra.

(12) *The urethro-cervical and cervico-trigonal fixing tissues.* Normally there is a firm fascial layer between the bladder neck and the cervix. This fixation becomes loosened in pregnancy and may be torn during labour. This will result in loss of the posterior urethral angle, as

described by Jeffcoate and Roberts. The anatomical basis of this angulation is described. The intrinsic muscle of the bladder and urethra runs parallel to the urethro-cervical fixing layer. At rest the intrinsic muscles and the fixing tissues work in opposition. During micturition the urethro-cervical fascia and the longitudinal and spiral muscles of the urethra are relaxed. The powerful levator ani holds the bladder base and neck in position. If this is weakened, or there is weakness of the smooth muscle of the fixing tissues, the normal topography is disturbed. Operations designed to repair the bladder neck and base and to restore the posterior urethral angle include the "tobacco-pouch stitch" of Meyers, Peham and Amreich, and others.

(13) *Fixation to the bladder.* The spiral and longitudinal muscles of the upper urethra are continuous with those of the bladder wall. In cases of prolapse the length of the urethra is reduced, and this of itself may cause incontinence. During micturition the upper part of the urethra is taken up into the bladder base. The para-urethral fixation of the upper urethra controls the movement of the bladder in filling and emptying.

To correct incontinence proper fixation of the bladder within the true pelvis must be secured. Three structures hold the bladder in the pelvis: (1) The levator ani muscle and the pelvic fascia of the bladder base which close the genital hiatus. (2) The fixation tissues between the bladder and the cervix. (3) The fixation layer between the bladder and the parametrium, with its extension over the ureters and so-called pillars of the bladder. A fourth ventral attachment is the pubo-vesical or pubo-cervical fascia which is continuous with the fascia lining the cave of Retzius, this running between the bladder and the pubic bone.

If there is marked descent of the bladder and urethra, with shortening of the urethra, then the operative procedure must be designed to repair all the fixing structures and to restore the normal length of the urethra. Sling operations lift the bladder neck, restore the posterior angulation of the urethra and tighten the longitudinal muscle of the urethra. Retropubic suspension of the bladder and urethra is successful in other cases. The best results are obtained by combined procedures designed to elevate the bladder and uterus, as in the Manchester repair, in vaginal hysterectomy and repair, or the interposition operation. A special type of ball pessary may be used with the same effect.

Josephine Barnes

57. **The Relationship Between Urethral Resistance and Chronic Urinary Tract Disease in Women.**

By D. M. Davis. *J. Urol.*, **76**, 270–275. Sept. 1956. 3 tables.

Davis points out that contracture of the bladder neck and narrowing of the urethra are common causes of cystitis in women. Narrowing of the urethra is easily diagnosed by passing a graduated series of bougies (the urethra should admit an F28 bougie). Oedematous tags at the bladder orifice are frequently seen on cystoscopy, as well as trabeculation of the bladder wall. Suprapubic pain, renal pain and digestive disturbances, in addition to the usual disorders of micturition, are found. Relapse after treatment is the rule.

Results of the treatment of 165 cases are given: all had dilatation of the urethra, 54 had fulguration of the oedematous tags, and 40 had endoscopic resection of the bladder neck. A Kollmann dilator was employed for the dilatation, and in some cases the urethra was dilated up to 45 F.

The importance of this subject to gynaecologists and urologists is very obvious. The ordinary narrow bore observation cystoscope is of no use in the diagnosis of these cases. The flushing cysto-urethroscope or a urethroscope, should be employed. The dangers of vesico-vaginal fistula as a result of inexpert use of the resecto-scope are very great. No mention is made of the estimation of residual urine in these patients—a common finding in bladder neck contraction.

[Davis is in error in saying that Mercier's bar is the thickened posterior lip of the vesical orifice. Mercier's bar is the inter-ureteric ridge and contraction of the bladder orifice due to chronic inflammation has long been known as Marion's disease.]

J. H. Carver

58. **Frequency in the Female Due to Urethro-Trigonitis Caused by Intestinal Infection.**

By J. E. Semple. *Brit. med. J.*, **2**, 696–697. Sept. 22, 1956. 3 refs.

The author, from St. Paul's Hospital, London, reviewed the incidence of urethro-trigonitis among females attending a urological clinic and found it to be 25 to 30 per cent. It occurred in any age group. Frequency of micturition occurred in 80 per cent of these patients, dysuria and urgency in 50 per cent. Chronic cervicitis was present in 66 per cent of these patients. In the remaining 34 per cent, in which no disease of the genital organs could be found, investigation of the large intestine was made. Out of 43 such patients, barium enema examination showed lesions in eleven, especially diverticulitis. The author suggests that infection might easily spread via the lymphatics to the bladder trigone in these patients. Treatment of the intestinal infection, combined with urethral dilatation and fulguration of the bladder neck when necessary, gave very good results.

Eileen Wilson

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The Editor is: Professor James Young, *D.S.O.*, M.D., F.R.C.S., F.R.C.O.G., Paynes Hill House, Steeple Aston, Oxford.

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Brown, H. E., and Jones, B. K. (1943): *J. Obstet. Gynaec. Brit. Emp.*, **2**, 128.

Sampson, P. (1940): *Obstetrics for Midwives*. 2nd edition. Fraser, London. p. 9.

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